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CHAPTER 6

The Care and Use of Hibernating Mammals[1]

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Hibernation may be defined as a physiological state which is cyclic, usually seasonally linked, and is characterized by reduction of many processes of the body to minimal levels. For example, deep body temperature may fall to a low level, approximating ambient temperature. Metabolic rate is drastically reduced, as are heart rate, respiratory rate, and other parameters (Hock, 1960b).

Hoffman (1964) has added to the above definition that spontaneous or induced arousal from this condition to normal levels is possible at all times. This serves to restrict the definition to homoiotherms, as the poikilotherms are not capable of arousal except that incident upon ambient temperature increase.

The subject has been reviewed by Johnson (1931a), Hoffman (1964), Lyman and Chatfield (1955), Kayser (1950a, 1957a, 1961a, 1965), Lyman (1961, 1963), Eisentraut (1956), Suomalainen (1956, 1962), Hock (1958a), and in the proceedings of the First International Symposium on Natural Hibernation (Lyman and Dawe 1960).[2]

It has been pointed out (Hock, 1958a; Lyman and Chatfield, 1955) that the word hibernation lacks precise meaning, and may in fact be applied to many groups of animals, such as insects, molluscs, reptiles, and mammals with entirely different connotations. Even if we restrict the discussion to mammals, there are several gradations of conditions of torpor which may be considered as comprising or approaching hibernation. The condition defined above is deep hibernation, and is one end of the spectrum of states comprising or resembling hibernation and usually lumped under this term.

I. Hibernation

Perhaps the essence of hibernation is the reduction of energy expenditure allowed by the lowered body temperature. Although this reduction of temperature and thus energy varies for different mammals exhibiting the various states (see Fig. 1), all lead to the same end of conserving energy reserves. It appears likely that hibernation arose independently in the several lines of mammals in which it is exhibited, and that this may have been a method of passing periods of food shortage. It does not appear that hibernation is a primitive condition due to imperfect temperature regulation.

Food is stored by most hibernators in the form of fat deposits, but the

[2]The Proceedings of the Second International Symposium on Natural Hibernation, held in Helsinki in 1962, have been published (Suomalainen, 1964). This volume should be referred to for information on many of the topics touched on in this chapter.

golden hamster actually stores food supplies (Lyman, 1954). Therefore, one of the most obvious phenomena associated with hibernation is the increase of the animal's weight just prior to the onset of hibernation, due to rapid fat deposition. Figure 2 shows this for wild Arctic ground squirrels.

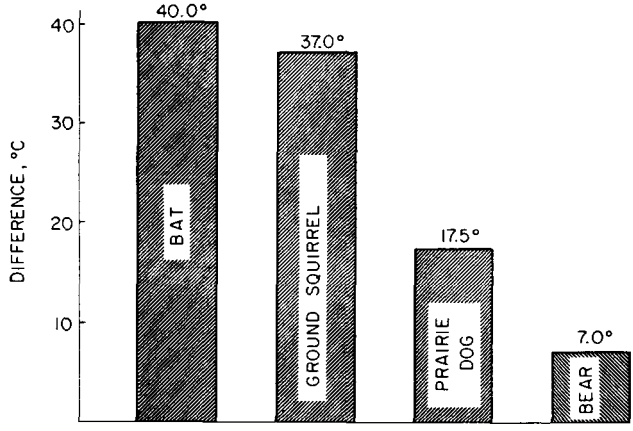

FIG. 1. Difference in deep body temperature of various species during activity and during hibernation. The temperature, in °C, is that found during hibernation subtracted from the temperature of the active animal. Reprinted, with permission, from Hock (1958b).

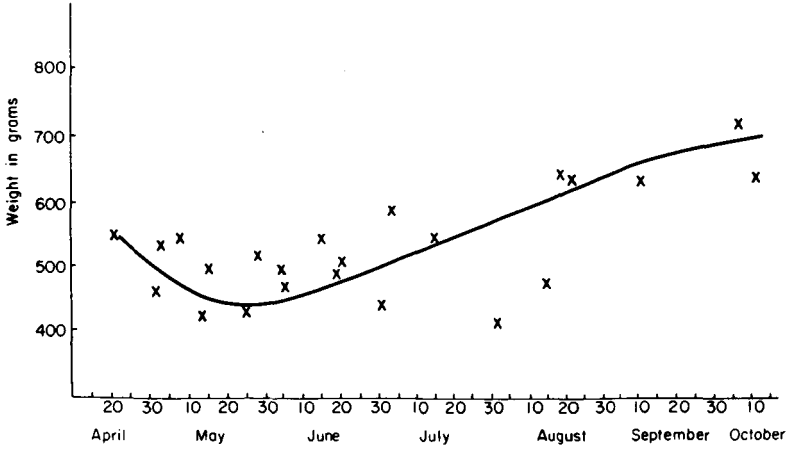

FIG. 2. Average weights of Arctic ground squirrels throughout their active season. × marks average for one date in 1 year; data are over a 5-year period. Reprinted, with permission, from Hock (1960a).

The decrease in deep body temperature allows a great decrease in the metabolic rate (MR) of the hibernator. For example, a ratio of 150 : 1 is found between the maximum MR of the little brown bat at 41.5°C ambient temperature (and presumably nearly the same body temperature), and the minimum rate found at 2°C (Fig. 3). The presumption that the body temperature is nearly the same as the ambient temperature in these bats is based upon data shown in Fig. 4.

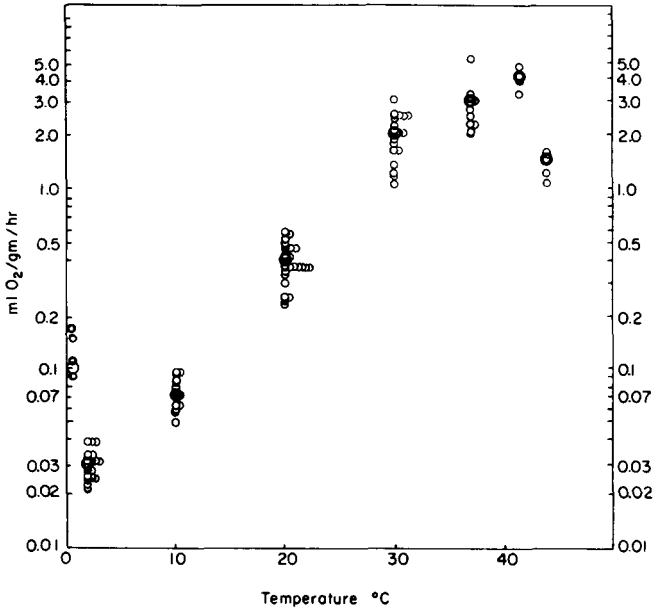

FIG. 3. Oxygen consumption of *Myotis lucifugus* in relation to ambient temperature. Reprinted, with permission, from Hock (1951).

Other studies have shown similar reductions in MR between active (i.e., nonhibernating) mammals and the same species in hibernation. In Arctic ground squirrels, for example, a ratio of 30 : 1 is found for animals active at 10°C as compared with animals hibernating at the same ambient temperature. The difference is that the active animals had body temperatures around 38°C, the hibernators around 10°C.

Many other physiological functions vary in hibernators when they are hibernating as compared to when they are active. These will be discussed under the "Techniques" section of this chapter, or cited for further reference.

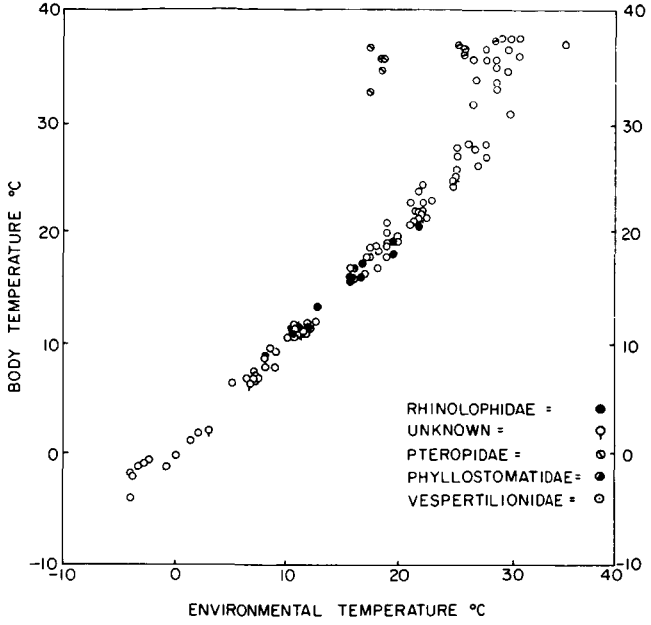

FIG. 4. Body temperature of bats of various families in relation to ambient temperature. Reprinted, with permission, from Hock (1951).

II. Mammals That Hibernate

Representatives of three orders of mammals show deep hibernation: the Insectivora, or insectivores; the Chiroptera, or bats; and the Rodentia, or rodents. In addition, many species of these groups show states resembling hibernation. The Carnivora, or carnivores, have species that exhibit a torpor, not deep hibernation. The Monotremata, Marsupalia, and Primata have all been reported to show torpor in at least one species. Table I is an attempt to summarize these states, and the mammals which exhibit them.

Some definitions of the various conditions listed in Table I are required. *Deep hibernation* is the condition defined above, in which body temperature approximates a low ambient temperature. The term *torpor* is used to characterize a state in which body temperature, heart rate, metabolic rate, and other parameters are reduced, but not as drastically as in deep hibernation. *Dormancy* is an even less well-defined state, and is used here to indicate some reduction in physiological levels, or denote lack of precise knowledge on the species in question. It should be stated here that information as to whether a given species hibernates or exhibits

TABLE I

MAMMALS WHICH HIBERNATE, OR SHOW RELATED CONDITIONS

Common name	Scientific name	Geographical distribution	Condition exhibited	Authority
		ORDER MONOTREMATA		
Spiny anteater	*Tachyglossus aculeatus*	Australia	Torpor	Wardlaw (1915)
Platypus	*Ornithorhyncus paradoxurus*	Australia	Torpor	Fleay (1944)
		ORDER MARSUPALIA		
Pigmy opossum	*Cercartus nanus*	Australia	Torpor	Bartholomew and Hudson (1962)
Pigmy glider	*Acrobates pygmaeus*	Australia	Torpor	Troughton (1931)
Koala	*Phascolarctos cinereus*	Australia	Torpor	Krumbiegel (1955)
Fat-tailed sminthopsis	*Sminthopsis crassicaudata*	Australia	Torpor	Findlayson (1933)
Virginia opossum	*Didelphis virginianus*	United States	Torpor (?)	Wiseman and Hendrickson (1950)
Murine opossum	*Marmosa* sp.	South America	Torpor	Morrison and McNab (1962)
		ORDER INSECTIVORA		
Tenrec	*Tenrec ecaudatus*	Madagascar	Deep hibernation	Eisentraut (1955)
"Hedgehog" tenrec	*Setifer* sp.	Madagascar	Deep hibernation	Lachiver, cited by Kayser (1961a)
Hedgehog	*Erinaceus europeaus*	Europe	Deep hibernation	Suomalainen (1960)
Saharan hedgehog	*Parechinus aethiopicus*	Africa	Deep hibernation	Eisentraut (1952) Lachiver, cited by Kayser (1961a)

ORDER CHIROPTERA				
Lesser horseshoe bat	*Rhinolophus hipposideros*	Europe	Deep hibernation	Eisentraut (1957)
Greater horseshoe bat	*R. ferrum-equinum*	Europe	Deep hibernation	Eisentraut (1957)
Barbastelle	*Barbastella barbastellus*	Europe	Deep hibernation	Eisentraut (1957)
Big brown bat	*Eptesicus fuscus*	No. America	Deep hibernation	Evans (1938)
Serotine	*E. serotinus*	Europe	Deep hibernation	Eisentraut (1957)
Keen bat	*Myotis keenii*	No. America	Deep hibernation	Evans (1938)
Little brown bat	*M. lucifugus*	No. America	Deep hibernation	Hock (1951)
Mouse-eared bat	*M. myotis*	Europe	Deep hibernation	Eisentraut (1957)
Bechstein bat	*M. bechsteini*	Europe	Deep hibernation	Eisentraut (1957)
Cave bat	*M. velifer*	W. No. America	Deep hibernation	Reeder and Cowles (1951)
Noctule	*Nyctalus noctula*	Europe	Deep hibernation	Eisentraut (1957)
European pipistrelle	*Pipistrellus pipistrellus*	Europe	Deep hibernation	Eisentraut (1957)
Eastern pipistrelle	*P. subflavus*	E. No. America	Deep hibernation	Evans (1938)
Western pipistrelle	*P. hesperus*	W. No. America	Deep hibernation	Hock (1960c)
Long-eared bat	*Plecotus auritus*	Europe	Deep hibernation	Eisentraut (1957)
Murine bat	*Vespertilio murinus*	Europe	Deep hibernation	Eisentraut (1957)
Free-tail bat	*Tadarida brasiliensis*	W. No. America	Torpor	Herreid (1963a,b,c)
California mastiff bat	*Eumops perotis*	S. W. No. America, Central and No. So. America	Torpor	Leitner (1961)
ORDER CARNIVORA				
Black bear	*Ursus americanus*	No. America	Torpor, "carnivorean lethargy"	Hock (1958a)
Grizzly bear	*U. horribilis*	Northern No. America	Torpor (?)	Holzworth (1930)
No. American brown bear	*Ursus* spp.	Northern No. America	Torpor (?)	Holzworth (1930)
European brown bear	*U. arctos*	Northern Europe	Torpor	Lobatchev (1951)
Polar bear	*Thalarctos maritimus*	Circumpolar	♀ torpid when pregnant	Koettlitz (1902) Pedersen (1945)

(*Continued*)

TABLE I–*Continued*

MAMMALS WHICH HIBERNATE, OR SHOW RELATED CONDITIONS

Common name	Scientific name	Geographical distribution	Condition exhibited	Authority
		ORDER CARNIVORA–*Continued*		
Striped skunk	*Mephitis mephitis*	U.S., Canada	Dormancy	Cuyler (1924)
European badger	*Meles meles*	Europe	No temperature reduction-dormancy	Johansson (1957a)
No. Am. raccoon	*Procyon lotor*	No. America	As above (?)	Eisentraut (1953)
Raccoon-like dog	*Nyctereutes procyonoides*	Eurasia	As above (?)	–
		ORDER PRIMATA		
Mouse lemur	*Cheirogaleus medius*	Madagascar	Dormancy (?)	Bourlière (1952)
Mouse lemur	*C. major*	Madagascar	Dormancy (?)	Bourlière (1952)
Mouse lemur	*C. milli*	Madagascar	Dormancy (?)	Kaudern (1914)
		ORDER RODENTIA		
Hoary marmot	*Marmota marmota*	Europe	Deep hibernation	Kayser (1961a)
Hoary marmot	*M. caligata*	No. America	Deep hibernation	Hall and Kelson (1959)
Woodchuck	*M. monax*	E. No. America	Deep hibernation	Lyman (1958a)
Baibac	*M. bobac*	Siberia	Deep hibernation	Kalabukhov (1956)
Siberian marmot	*M. siberica*	Siberia	Deep hibernation	Kalabukhov (1956)
Yellow-bellied marmot	*M. flaviventris*	W. No. America	Deep hibernation	Hock (1963)
	M. caudata	U.S.S.R.	Deep hibernation	Kalabukhov (1956)
Black-tailed prairie dog	*Cynomys ludovicianus*	W. United States	Dormancy	Hall and Kelson (1959)
White-tailed prairie dog	*C. leucurus*	W. United States	Dormancy	Hall and Kelson (1959)

ORDER RODENTIA—*Continued*

Suslik	*Citellus citellus*	No. Europe	Deep hibernation	Kayser (1961a)
Large ground squirrel	*C. major*	U.S.S.R.	Deep hibernation	Ognev (1947)
Yellow ground squirrel	*C. fulvus*	U.S.S.R.	Deep hibernation	Kalabukhov (1956)
Small ground squirrel	*C. pygmaeus*	U.S.S.R.	Deep hibernation	Kalabukhov (1956)
13-lined ground squirrel	*C. tridecimlineatus*	Middle United States	Deep hibernation	Johnson (1931a)
Columbian ground squirrel	*C. columbianus*	W. United States	Deep hibernation, estivation	Shaw (1925a)
Townsend ground squirrel	*C. townsendii*	W. United States	Deep hibernation, estivation	Hall and Kelson (1959)
Beechey ground squirrel	*C. beecheyi*	W. United States	Hibernation	Strumwasser (1959a)
Golden-mantled ground squirrel	*C. lateralis*	W. United States	Deep hibernation	Pengelley and Fisher (1961)
Arctic ground squirrel	*C. undulatus*	Alaska, Siberia	Deep hibernation	Hock (1960a)
Mohave ground squirrel	*C. mohavensis*	Mohave Desert, California	Hibernation, estivation	Bartholomew and Hudson (1960)
White-tailed antelope ground squirrel	*C. leucurus*	W. United States	Does not hibernate or estivate	Bartholomew and Hudson (1961)
Richardson ground squirrel	*C. richardsonii*	W. United States	Deep hibernation	Hall and Kelson (1959)
Belding ground squirrel	*C. beldingi*	W. United States	Deep hibernation	Hall (1946)
Franklin ground squirrel	*C. franklinii*	United States	Deep hibernation, estivation	Dawe and Morrison (1955)
Round-tailed ground squirrel	*C. tereticaudus*	W. United States	Torpor	Hudson (1962)
Eastern chipmunk	*Tamias striatus*	E. No. America	Torpor, can achieve deep hibernation	Panuska (1959)
Long-eared chipmunk	*Eutamias quadrimaculatus*	W. No. America	Torpor	Cade (1963)
Least chipmunk	*E. amoenus*	W. No. America	Torpor, can achieve deep hibernation	Cade (1963)
European hamster	*Cricetus cricetus*	Europe	Deep hibernation	Kayser (1961a)

(*Continued*)

TABLE I–*Continued*

MAMMALS WHICH HIBERNATE, OR SHOW RELATED CONDITIONS

Common name	Scientific name	Geographical distribution	Condition exhibited	Authority
		ORDER RODENTIA–*Continued*		
Golden hamster	*Mesocricetus auratus*	Middle East	Deep hibernation	Kayser (1961a)
	M. raddei	U.S.S.R.	Deep hibernation	Kalabukhov (1956)
	Cricetulus triton	U.S.S.R.	Torpor	Loukashkin (1944)
Lesser Egyptian gerbil	*Gerbillus gerbillus*	No. Africa	Torpor	Petter (1955)
Egyptian gerbil	*Meriones tristrami*	No. Africa	Torpor	Petter (1955)
Forest dormouse	*Dryomys nitedula*	Europe	Deep hibernation	Kayser (1961a)
Fat dormouse	*Glis glis*	Europe	Deep hibernation	Kayser (1961a)
Garden dormouse	*Eliomys quercinus*	Europe	Deep hibernation	Kayser (1961a)
Japanese dormouse	*Glirulus japonicus*	Japan	Deep hibernation	Shimoizumi (1943)
Common dormouse	*Muscardinus avellanarius*	Europe	Deep hibernation	Kayser (1961a)
Birch mouse	*Sicista betulina*	N. Europe	Deep hibernation	Johansen and Krog (1959)
	S. subtilis	U.S.S.R.	Deep hibernation	Ognev (1947)
Meadow jumping mouse	*Zapus hudsonicus*	N. No. America	Deep hibernation	Sheldon (1938a)
Woodland jumping mouse	*Napaeozapus insignis*	N. No. America	Deep hibernation	Sheldon (1938b)
	Allactaga jaculus	Africa	Deep hibernation	Kalabukhov (1960)
Siberian 5-toed jerboa	*A. siberica*	U.S.S.R.	Deep hibernation	Kalabukhov (1960)
Jerboa	*A. elater*	U.S.S.R.	Deep hibernation	Kalabukhov (1960)
Jerboa	*A. acontion*	U.S.S.R.	Deep hibernation	Kalabukov (1956)
Jerboa	*Scirtopoda telum*	U.S.S.R.	Deep hibernation	Kalabukov (1956)
Northern 3-toed jerboa	*Dipus sagitta*	Sw. U.S.S.R.	Torpor	Ognev (1947)
Lesser Egyptian jerboa	*Jaculus jaculus*	North Africa	Torpor	Petter (1955)
Little pocket mouse	*Perognathus longimembris*	W. No. America	Torpor	Bartholomew and Cade (1957)
California pocket mouse	*P. californicus*	California	Torpor	Tucker (1962)

ORDER RODENTIA—*Continued*

Merriam pocket mouse	*P. merriami*	W. No. America	Torpor	Cade (1964)[a]
Yellow-eared pocket mouse	*P. xanthonotus*	W. No. America	Torpor	Bartholomew and Cade (1957)
Long-tailed pocket mouse	*P. formosus*	W. No. America	Torpor	Bartholomew and Cade (1957)
San Diego pocket mouse	*P. fallax*	W. No. America	Torpor	Bartholomew and Cade (1957)
Pale kangaroo mouse	*Microdipodops pallidus*	W. No. America	Torpor	Bartholomew and MacMillen (1961)
Merriam kangaroo rat	*Dipodomys merriami*	W. No. America	Dormancy (?)	Dawson (1955)
Northern pygmy mouse	*Baiomys taylori*	Sw. United States	Torpor	Hudson (1963)
Cactus mouse	*Peromyscus eremicus*	W. United States	Estivation	MacMillen (1964)
Deer mouse	*P. maniculatus*	No. America	Lack of thermoregulation when chilled, not dormancy	Sealander (1953)

[a]Cade (1964) has discussed many other species of rodents that show some degree of torpidity. His paper should be referred to by those interested.

one of the related conditions is known for the most part only for those species inhabiting North America or Europe. Even here, especially in North America, there are some species that may show one of these phenomena, but which are not in the tables. This is true of some ground squirrels, for example, and denotes lack of an authoritative reference to the fact. For many of the rest of the world's mammalian species, no knowledge is available as to whether or not they hibernate or show one of the similar conditions.

III. Types of Mammalian Hibernation

There are perhaps as many "types" of hibernation as there are species that hibernate, for one or more parameters will vary in each different species. However, an attempt will be made here to discuss the major conditions comprising this and related states and to classify them. This may conveniently be done by using a phylogenetic approach.

First, we may consider that some bats hibernate, especially members of the families Vespertilionidae and Rhinolophidae, widely distributed in Europe and North America. These bats also drop their body temperature daily, when they are at rest (Hock, 1951, 1958a). It thus appears that these bats are distinct from other mammalian hibernators, and this daily condition has been called "diurnation" or "*Tageschlafiethargie.*" There seems to be no real difference between the bat in this condition of daily temperature reduction and consequent torpor, and the bat in hibernation. However, due to this obvious distinction between the thermoregulatory ability of these bats and the other mammals, even the hibernators, the term "obligatory mammalian hibernation" has been proposed for this phenomenon (Hock, 1958a). This serves to indicate that these bats must lower body temperature when ambient temperature is low, but they do not go into seasonal hibernation unless the preparation for that process has been achieved (Menaker, 1962). On the other hand, it serves to distinguish them from the poikilotherms, which also lower their body temperature as a response to lowered ambient temperature but which, unlike the bats, cannot spontaneously raise their body temperature in a cold environment and thus arouse from hibernation.

The bear is widely reputed to be a hibernator. From studies made in Alaska (Hock, 1957, 1958a), it is apparent that the degree and depth of the phenomenon in the black bear, as judged from colonic temperature and metabolic rate (Hock, 1960b), is not that of what Lyman and Chatfield (1955) have called "deep hibernation" (see Figs. 5 and 6). It has been suggested (Hock, 1958a) that the condition found in the black bear, and presumably present in other bears and perhaps other carni-

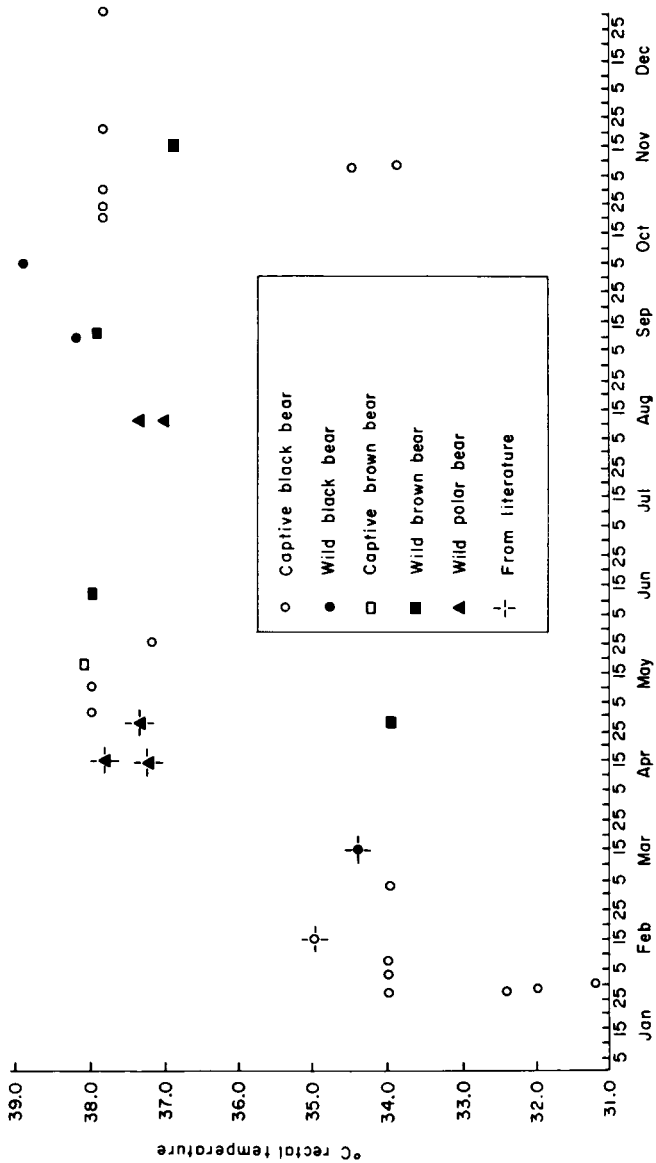

FIG. 5. Colonic temperatures of various species of bears throughout the year, active and "hibernating." Reprinted, with permission, from Hock (1958a).

vores, be called "carnivorean lethargy" to distinguish it from more profound hibernation. Morrison (1960) has said that it appears that the black bear is an ecological, but not a physiological, hibernator. He shows a family of curves indicating that the black bear does not have to reduce body temperature as drastically as do the rodent hibernators, due to its larger size, greater fat stores, and lower thermal conductance.

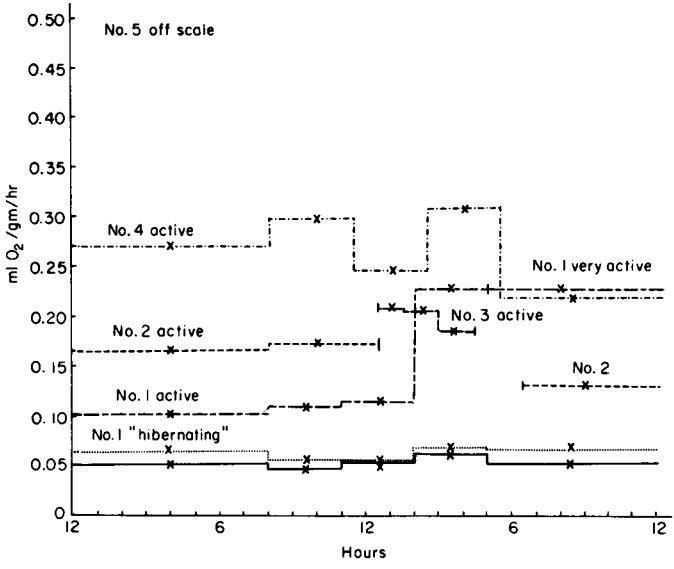

FIG. 6. Metabolic rate of black bears, active and "hibernating." Reprinted, with permission, from Hock (1960a).

It is in the rodents that what may be regarded as the quintessence of hibernation is found. This condition has been called "typical hibernation" or "true hibernation," but it has been pointed out that such terminology implies that other types or degrees of hibernation are false or atypical. Therefore, the term "deep hibernation" (Lyman and Chatfield, 1955), will be used, although the author regards this condition as perhaps the ultimate attainable by mammals. This is the state in which deep reduction of the body temperature, metabolic rate, heart rate, and other physiological functions is found. More studies have been made on the mammals exhibiting this phenomenon than on those which exhibit any of the other physiological states which comprise what is usually considered as hibernation. For this reason, most of the discussion and references in the "Techniques" section will refer to "deep hibernation."

IV. Environmental Factors

Common usage attributes the cause of hibernation to the onset of seasonal cold, but once again common usage is wrong. The fact is that most species hibernate before cold weather. Food shortage appears to be the reason for the development of hibernation, and this may well be true in the historical sense. However, many species enter hibernation in the presence of abundant food. Furthermore, food deprivation gives contradictory results when used to cause animals to enter hibernation. Some of this contradiction is due to the species used, and some may be due to differing experimental conditions.

The search for real and measurable environmental stimuli has thus far proved unrewarding. This is partly due to the fact that a given stimulus which acts on one species may not act so on another species or, indeed, even on the same species in a widely divergent habitat. Thus, cold may indeed cause one species to enter hibernation, restriction of food may cause another to do so, but no universal stimulus acting on all hibernating species is apt to be demonstrated. The daily photoperiod is proposed as the environmental stimulus acting on Arctic ground squirrels, due to the precision with which they enter hibernation (Hock, 1955). Although not proved experimentally, unseasonally early fattening due to artifically decreasing day length was demonstrated. In those animals which deposit fat stores prior to hibernation, it appears that such fattening is necessary for the onset of normal hibernation.

The search for an external stimulus for hibernation may be further complicated by the fact that although students of hibernation are looking for an environmental "trigger" which causes a nearly immediate onset of hibernation, the environmental stimulus may in reality act earlier in the season, and serve as a cue which starts the preparation for hibernation. In the case of the Arctic ground squirrel, it is possible that day length acts not to initiate the entrance into hibernation, but may in fact act much earlier in the season, and cause fattening or endocrine involution, or some other part of the preparation for hibernation. This process or processes in turn may provide the internal "trigger" which initiates hibernation.

Pengelley and Fisher (1957, 1963) found that at constant photoperiod and ambient temperature golden-mantled ground squirrels maintained their annual weight cycle for up to 2 years. Furthermore, unseasonal hibernation could not be induced by changing photoperiod, but could be induced by causing animals to shift their weight through ambient temperature manipulation.

Kayser (1952a, 1961b) has treated other parameters in internal versus external factors determining hibernation.

V. Hibernation versus Hypothermia

In recent years, the advent of hypothermia as a surgical adjunct has received much attention. Unfortunately, this has been called "hibernation" in the medical literature, or at best "artificial hibernation." It is therefore essential to distinguish between these two conditions.

Hypothermia, or "artificial hibernation" has several attributes in common with the natural hibernation we are discussing. Chief among these, of course, is the reduction of body temperature found in both states, which is accompanied by a reduction in heart rate, metabolic rate, and other functions (Hock and Covino, 1958). However, hypothermia is an event for which the animal is not prepared, whether it is experimentally induced accompanying surgery, or the result of immersion in the ocean. It is, from the animal's viewpoint, an accident.

On the contrary, hibernation is a normal event in the hibernator's life. We can point up this distinction by alluding to ventricular fibrillation, which thus far is the barrier to more profound states of hypothermia in man, dog, and rat. It occurs at some body temperature more or less characteristic of the species, but usually near 25°C. On the other hand, natural hibernators normally hibernate near 2–5°C, without the advent of fibrillation.

Further references to this distinction are Fontaine (1953), Giaja (1953), Kayser (1955a,b, 1956, 1959b), and V. Popovic (1959, 1960b).

VI. Estivation

This phenomenon is widely reputed to be "summer sleep," a retreat from seasonal heat and/or lack of moisture. However, it had appeared to students of hibernation that its physiological characteristics were similar to those of "winter sleep." It remained for Bartholomew and Hudson (1960) to demonstrate this, which was done in a study of the Mohave ground squirrel. The main distinction seems to be that these animals enter estivation at a higher ambient temperature than that at which animals normally enter hibernation, and that the body temperatures tend to be much higher. See Hudson and Bartholomew (1964) for an excellent review of this phenomenon.

VII. Choice of Animal for Research

If an investigator is interested in using one of the hibernating species for research, he must first determine which of the types of phenomena

is most pertinent for him to utilize. Then from Table I he can select species most readily available. Obviously, if one wishes to study something concerned with bat rabies, the first segment of the choice is simple—a bat. For the second segment, the question becomes, what species of bat? If the investigator is North American or European, he may select one of the numerous species of rhinolophine or vespertilionine bats which are known to hibernate. If a choice can be made of a species that is locally available, one is most fortunate. On the other hand, for some specific problems one may find that exotic species are more desirable and recourse to a supplier may be necessary.

It cannot be too strongly stressed that the choice of a species for test animal is of paramount importance. It is increasingly apparent as more work is done on more species that the results of specific studies on one species are not necessarily applicable to another species. This is especially true when they are not closely related species, for example, hamsters and marmots. For help in the selection of the appropriate species, expert advice may be solicited. The Hibernation Information Exchange, comprising all the world's workers in this field (Dawe, 1961), may be consulted for such help. The address of this organization is 219 S. Dearborn St., Chicago, Illinois, 60604.

After the choice of species has been made, the worker should learn as much as possible about the species, in hibernation and in normal activity. This may be done by referring to Kayser (1961a), Lyman and Dawe (1960), and other works cited here.

VIII. Procurement of Animals

If the species selected is one found locally, the investigator may prefer to secure his own animals. Bats may be obtained in winter in caves or mine tunnels, where they may occur in large numbers. They are very easy to capture when they are hibernating. A note of caution is in order here. Although there may seem to be an inexhaustible supply present, the numbers of bats in most caves, as in northeastern United States, gather there from a wide area to hibernate. Thus only those actually needed should be taken. Even then, the avoidance of undue disturbance is necessary, as too great and too frequent disturbance may cause the colony to abandon the cave. Away from localities where there are caves, bats may be found in summer in attics, under bridges, or in other places, and may be taken there (Davis and Cockrum, 1963). See Griffin (1940) for methods of capturing bats.

Ground squirrels, chipmunks, woodchucks and some of the European species may be locally present, and can be live-trapped, using Toma-

hawk, Havahart, Sherman, or similar traps. It is essential that these traps be picked up early in the morning, as too long exposure to the sun will kill the animals. Also, of course, such trapping must be done during the active season of the animals. Thus trapping in the summer or early fall is necessary to insure a supply of animals for the subsequent winter. If the investigator himself does not wish to trap, a student or other helper may be hired. In this case, pay for animals trapped, not for time spent.

If the species selected is exotic, it may be obtained from various animal suppliers. Hedgehogs, dormice, and other animals are so supplied, although advance notice may be required. Hamsters may be taken from the local animal room stock. Reference to state or federal law is necessary here if shipment across state lines, or from one country to another, is involved. State game laws should be consulted prior to undertaking capture of any wild animals by the investigator or his agent.

IX. Care of Individual Species

There is a vast difference between adequate care for the common laboratory animals and care for hibernators such as to insure that they will hibernate. This difference consists largely of several details not usually observed in even the best "rat rooms." First, it is obvious that a temperature-controlled room is needed, preferably of the walk-in type, and capable of being kept for long periods of time at $5 \pm 1°C$. Second, this room should not have any noise that clicks on and off, like a compressor or circulating fan. Continuous quiet circulation of cooled air from outside is best, although good success can be had with a continuous circulating fan, the noise of which obscures the on-off cycle of the compressor. In cool climates one may merely heat by electrical means, but this usually requires a separate building, and that is often difficult.

The noise factor is of primary importance in the routine care of the animals. Animal caretakers are notoriously noisy, and the usual cart with rattling water bottles is enough to cause a serious disturbance. The investigator faced with this problem may find it better to detail a technician or other assistant to the care of the hibernators. Access to the hibernating quarters must be denied to all other people. Use a lock!

In all cases, except for bats, animals should be caged separately, as otherwise an animal in hibernation may be eaten by those that have not hibernated. Since the process of arousal usually takes some hours, an animal in hibernation is incapable of defense if attacked by a cagemate.

A. Bats

These animals are relatively easy to care for if short-term experiments are conducted. Then the bats need only be placed in a cold room ($5 \pm 1°C$) and kept, with provision made for adequate water, both for drinking and in the form of water vapor. The small size of bats causes them to dehydrate rapidly even in a cold environment. Water vapor may be provided by a vacuum pump line bubbling air through water in a glass bottle. Near saturation of the environment is advisable.

However, if periods longer than a few weeks are required the bats must be fed. This requires removing them to a warm room, and allowing body temperature to rise. A dish of "bat glop" should be provided. The recipe is as follows: equal parts by weight of hard boiled egg yolk, cottage or cream cheese, *ripe* banana, and live meal worms are ground in a Waring Blendor. Add 6 drops of liver extract (Jeculin) for each egg yolk, 6 drops of wheat germ oil, and 3 grains Theragran multivitamins. Mix enough for several feedings and freeze it in blocks, removing one block for feeding each time.

When bats are to be fed, be sure to provide low pans, such as petri dishes, in the container holding the bats. One container is for food, the other for water. Unfortunately, few bats learn to eat by themselves, and some will not learn even after a course of training. To teach a bat to eat, a small bolus of the food may be offered with forceps. The bat's nose must be touched with the food, and patience is required. If the bat eats, or one's patience is exhausted, it should be put in another container, until all bats have been fed as much as they will eat. Then they should be returned to the original container and put back in the cold room. This process should be repeated every week. The bats that do not eat will die.

The container for the bats should be made of ¼ or ½ inch hardware cloth, cylindrical in shape, and about 18 inches in circumference by 24 inches high. One hundred or more bats may be conveniently housed in this. Some means of preventing escape via the top must be provided, such as a folded-over cheesecloth sleeve with 4–6 inches of hard plastic sheet wrapped around the top of the wire and secured so the bats cannot crawl over it. If the bat container is to be kept in a large cold room, it may be wrapped with burlap or other material, and this kept wet. The container without burlap may be placed in an ordinary refrigerator, and an air line from a vaccum pump bubbled through water may be led into the container, and evaporation thus held down.

To induce hibernation, the bats have merely to be placed in a cold environment. This may work at any time of year, but the investigator

should be warned to state, in his results, the time at which he did his experiments. Menaker (1961, 1962) has brought forth information which indicates that summer torpidity may not have the same characteristics as winter hibernation, although in temperature response and oxygen consumption no seasonal differences were noted (Hock, 1951).

An excellent reference on the care of bats is Mohos (1961).

B. Hedgehogs

This author has no personal experience with these animals. However, Edwards (1957) describes the care of the European species. Presumably the other species listed under "Insectivora" in Table I, have care approximating that of this species. It is worth noting here that many people who keep animals other than the usual laboratory species often incorporate unusual items of food, housing, or some other facet of care into their routine. These are often nothing more than mere personal foibles, and may really have nothing to do with the animal's welfare. Such items include unusual foods, such as live earthworms for the present species, or the presence of a swing for birds. In general, it may be stated that the more routine, and therefore less filled with perhaps meaningless details, the care and maintenance of any animal colony the more successful is it apt to be. Especially is this true if large numbers of animals are to be used. This does not mean that any aspect of *essential* care can be omitted, and occasionally unusual care may be indulged in. But the aim of successful care is to provide food, caging, and other conditions conducive to optimum maintenance, and the more routine and less demanding these conditions can be made the more likely they are to be successfully carried out.

Unlike the bats, the hedgehog is a seasonal hibernator only, although it will to some extent drop its temperature when placed in summer in a cold environment. However, winter exposure to cold following a period of fattening gives best results. Temperatures around 10°C may well be used for the cold room.

C. Marmots

The several species of marmots, including the woodchuck, are easy to keep in captivity and are excellent, large hibernators. The cage is of utmost importance, for marmots can chew through a conventional mesh cage in minutes. Stamped metal, 2 inch concrete reinforcing wire, heavy wire mesh (as used for "burglar-proof" windows), or chain link

is suitable for cages, as long as they are not attached to wood inside, for this marmots really relish. Size of the cage should be at least $24 \times 24 \times 12$ inches, with $30 \times 30 \times 16$ inches preferable. A round earthenware dish 4–6 inches high, and so large as to be not easily tipped over, is adequate for water. Food may be simply rat pellets, of some good high protein brand. Dog pellets have been successfully used by the author. This is all the food required, but supplements of whole or cracked corn may be used, and lettuce, apples, and carrots are relished. Food consumption is large, so keep a good supply in the cage.

Most mammals do not need nest boxes if the environment is quiet. Also, of course, when a nest box is used, one cannot conveniently see whether the animal is hibernating or not, and a small disturbance is required to ascertain this. However, an amount of nonabsorbent cotton, paper towels, or other material can be added for nesting purposes.

It should here be stressed that marmots can give a severe, perhaps permanently damaging bite, and they are difficult to handle due to their size. BE CAREFUL! Of course they may easily be handled when they are hibernating.

Marmots are very easy to get into hibernation, provided they are adequately fat in the fall. They will eat more in late summer, and should be fed *ad lib*. Then, if they are placed in an atmosphere of 5–10°C and left as quiet as possible, success of hibernation is excellent.

D. Ground Squirrels

There are many species of the genus *Citellus*,[2] and the various species have differing hibernation patterns. Some species hibernate, some hibernate and estivate, and at least one species (*Citellus leucurus*) does

[2]Note on Nomenclature: Experimental scientists are rarely taxonomists, and often do not realize that the same species of mammal may have more than one name. For example, the Arctic ground squirrel has also been called the "Alaskan ground squirrel," "Barrow ground squirrel," "Parry's ground squirrel," etc. Scientific names are usually more stable, but the same animal, *Citellus undulatus*, has also been called *Citellus parryi*, *Citellus barrowensis*, and even *Spermophilus undulatus!* Some additional confusion has been caused by combinations of these names, such as *Spermophilus parryi barrowensis*. Some individual workers have even used two or more different names for this species. The confusion is caused by attempts on the part of experimental scientists to be taxonomists without regard for the fact that this field is fraught with peril. Let the taxonomists revise, and the experimentalists follow! The well-known and stable marmot has been called *Marmota* for many years. But in the older literature it is called "*Arctomys*," and in some European papers one can still read "*Arctomys monax*," sometimes accompanied by "*Marmota monax*."

Get help from a taxonomist, if needed, to follow the literature. And by all means, make no new names to confuse posterity! Be conservative in *your* use of a name.

neither. Due to the wide range in size, caging requirements vary. It may be stated that a suitable cage for one of these rodents should have several times the floor space occupied by the animal's body. Thus, for *Citellus tridecimlineatus* of the midwestern United States, or *C. lateralis* of the West, a cage of 16 × 9 × 9 inches is adequate, whereas for *C. undulatus* of Alaska and Siberia, *C. beecheyi* of California, and *C. citellus* of Europe a cage about 18 × 18 × 9 inches is preferable. Regular mesh cages with a front-opening door are excellent for this species, but must have a removable pan with a wire floor over it. Again, nest boxes are not used but a minimum amount of nest material for hibernation is provided.

These animals are kept with a minimum of care, although if they are to be expected to hibernate, the requirements, as to noise especially, are more rigid. It is important to keep only one animal in a cage in winter, as otherwise the first one to hibernate will be eaten by its cagemates. In summer several can be put together in larger cages out-of-doors. If this is done, nest boxes must be provided for retreat.

Ground squirrels live very well on rat pellets, dog pellets, rabbit or guinea pig chow, or similar food. Cracked corn is an excellent supplement to this diet, but much will be wasted. Water bottles should be provided, or an automatic watering system used. In lieu of this, a fourth of a head of lettuce may be fed each squirrel three times a week. A small carrot, or a piece of a larger one, can be given occasionally.

Squirrels add large amounts of fat preceding hibernation. Although the above diet should provide enough calories to allow for this, the following high caloric diet will assure this, and may be used at other times: 1000 gm Crisco or similar shortening, 1500 gm cane sugar, 1500 gm corn meal, 500 gm powdered skim milk, 750 gm peanut butter (occasionally), 50 gm cod liver oil. This should be thoroughly mixed, preferably with a beater, after first mixing the dry ingredients by hand. It can be packed into small cans, and cracked corn and pellets may be imbedded, if desired. Only enough for a few days should be placed before the squirrel. The above will feed 50–100 squirrels for 2 days, depending on size. It provides 495 calories per 100 gm, without the peanut butter. This may be added to give variety to the diet, but is not necessary. Feeding 3 times per week is ideal for ground squirrels.

It may be found that these animals will not fatten completely if they are in a year-round constant cold environment, especially if they are subject to a constant light regime. If it is inconvenient to move them in summer to a warmer environment exposed to a natural photoperiod, they may be fattened satisfactorily by raising the temperature of the room or by decreasing the photoperiod slowly.

The photoperiod is believed to be the environmental cue responsible for the onset of hibernation in the Arctic ground squirrel (Hock, 1955). At any rate, if the photoperiod is to be manipulated to induce fattening, it is probably well not to start with the setting of 12 hours usual in most light-controlled animal rooms, which is often imposed in lieu of any knowledge of a better period. The regime which starts at 12 hours, then decreases one-half hour per week from August 1, will result in an 8-hour period on October 1. The photoperiod to be utilized during the winter should not be less than that encompassing the hours when there may be disturbing entrances into the cold room, say 8 am to 6 pm. Therefore, if the photoperiod is to be controlled for fattening purposes, it should be started at 16 hours in June or July, then decreased to 10 hours by October.

There may be some reason to keep lights on for 24 hours a day. It has been found that the Arctic ground squirrel, kept in 24-hour light and 5°C all year, lost its cycle so that hibernation could occur at any time. (Mayer, 1953). Pengelley and Fisher (1963), however, found that *Citellus lateralis* maintained its annual hibernation schedule even when all environmental conditions were kept constant.

Temperature at which hibernation may occur best will perhaps vary in the different species, but it is usually 5–10°C. Control should be ± 1°C. High wind speed inside the cold room should be avoided, and a baffle around the circulating fan may be needed. Humidity does not seem to be critical, but should be about 60% RH or higher. If doors are opened at least once *each* day, air does not usually need to be pumped into the cold room. Twenty-five Arctic ground squirrels can be kept in $6 \times 6 \times 7$ foot "reefers" with no difficulty, and with air supplied only by opening doors. One must be watchful for failure of the cooling apparatus, for when this occurs, temperatures rise rapidly and the animals consume much greater amounts of exygen, and consequently may die.

Ground squirrels may be bred in captivity, although the difficulties are usually greater than the gains. The pair to be mated must be put together right after cessation of hibernation, when the male has scrotal testes. After a week the male should be removed. Gestation period is about 25 days.

E. Chipmunks

These rodents may be cared for according to the general scheme given for ground squirrels. Cages may be the $9 \times 9 \times 15$ inch size, and sunflower seeds added to the diet, for in general these rodents require

greater diversity of food than do ground squirrels. They are very active, and exercise wheels may be needed. If there is a delay in the onset of hibernation, these wheels should be removed. It should be reemphasized here that chipmunks may not go into "deep hibernation" (Panuska, 1959; Cade, 1963; Woodward and Condrin, 1945).

F. Hamsters

Excellent instructions for the care of these rodents are available in several books (cf. Hindle and Magalhaes, 1957); therefore, only the added care needed to get them to hibernate will be discussed.

The first rule is that hamsters must have an adequate food store, as they do not deposit fat on their bodies, but must accumulate large amounts of food (Lyman, 1954). Therefore, the "clean cage" practice is not good. Also, solid floor cages with large amounts of litter are necessary rather than mesh floors.

Even when these conditions are met, hamsters will usually remain active in the cold room for a lengthy period. Part of this time is utilized in converting body fat to a less saturated form with lower melting point (Fawcett and Lyman, 1954). Thus, one should place the hamsters in the cold, overfeed, and wait. However, hamsters are not cyclic hibernators, and so may be induced to hibernate at any time of year, which is an obvious advantage. Temperature of the cold room should be 5°C, and noise is especially to be avoided for successful hibernation of this species.

G. Dormice

Several genera and species of these animals hibernate. The only one with which the author has had experience is *Myoxus avellanarius*, but it appears that care of all species is similar. Thomson (1957) has a chapter on *Glis glis*, the edible or fat dormouse, and this should be referred to.

Dormice may be caged in small cages, $9 \times 9 \times 15$ inches or larger. They are very quick and active animals, and one should be careful to see that the door is of the quick-closing type. They do not appear to be pugnacious, and several may be kept in a larger cage. However, this should not be done during hibernation. They may be provided with a nest box.

Food consists of apples or other fruits, dog biscuit or pellets, rat pellets, sunflower seed or nuts. Water must be provided *ad lib.*

The species kept in this laboratory is an excellent hibernator and, in addition, whenever cold temperature exposure occurred, torpidity resulted. One must, of course, distinguish this from natural hibernation. An ambient temperature of 5–10°C is recommended.

H. Jumping Mice

Mice of the genera *Zapus* and *Napaeozapus* in North America, and *Dipus, Jaculus,* and *Sicista* of Europe, Asia, and the Middle East seem to require similar care. Stock colonies may be housed in large aquaria with much litter (Morrison and Ryser, 1962), but individual mice should be put in separate jars or cages for study. Rat, rabbit, or guinea pig pellets, sunflower seeds, corn, an occasional bit of carrot, and water should be provided.

These mice fatten remarkably—up to 100%—in advance of hibernation, so excess food must be provided. Ambient temperatures of 10°C are recommended for hibernation. Schwentker (1957) discusses routine care of these animals.

I. Pocket Mice and Kangaroo Mice

Members of the family Heteromyidae have been found to hibernate, but probably only under special conditions (Bartholomew and Cade, 1957; Bartholomew and MacMillen, 1961). Pocket mice of the genus *Perognathus* offer possibilities for general study, because of the many widely distributed species occurring under a wide variety of climatic conditions throughout the southwestern and western United States. The kangaroo mice, *Microdipodops,* have very restricted distributions, occurring only in a few desert areas.

Both kinds of mice can be kept individually in small jars or terraria with an inch or more of fine sand on the bottom. They should be fed mixed bird seed, supplemented in the case of the kangaroo mouse with an occasional piece of cabbage or other succulent vegetable. They do not need water, and probably will not take it if provided.

Pocket mice *may* enter hibernation when placed at 5–10°C for 10 days or so, with food available. However, hibernation can be induced within 24 hours by removing food while the animals are exposed to this temperature. Kangaroo mice may become dormant at higher temperatures with food available, and this will occur at any time of year, and at temperatures of 5–26°C. However, if food is removed, the mice will enter hibernation within 24 hours at these same temperatures. Note that these mice can be thus induced to hibernate at any time of year,

and do not require a period of preparation prior to hibernation. Caution in needed in interpreting this phenomenon as being characteristic of normal, that is seasonal, hibernation as found in other species.

J. Bears

These mammals are not recommended for research, due to: (1) the fact that they rarely go into a lethargic condition until they are in their second winter, or later (some may never do so); (2) the expense of feeding and care; (3) the large amount of room needed per animal; (4) the difficulty in getting them, which when coupled with the time and money invested, means that large numbers cannot be used; (5) their difficult temperaments, and the consequent danger in keeping and handling them.

Other carnivores have been considered as perhaps showing this phenomenon of "carnivorean lethargy" (Hock, 1958a). These are the striped skunks, the raccoon, the European badger, and the raccoon-like dog, *Nyctereutes procyonoides* of Eurasia. Eisentraut (1931, 1953) states that the raccoon and badger do not hibernate. Various attempts to get the skunks to do so have failed in several U. S. laboratories. It therefore appears that there may be no "easy road" by means of use of these smaller animals to study lethargy in carnivores. Lehtonen (1948) found that some European brown bears in zoos did exhibit lethargy, while some did not.

Bears should be kept in heavily barred cages about $8 \times 8 \times 6$ feet or 8 feet high, as a minimum. This is true for adult bears; several cubs can be kept together, and pairs may be kept in a single cage for a few years. If cages can be larger, say 12×12 feet, this is advisable. Several cages side by side with doors between allow easy shuffling of bears back and forth for cleaning, feeding, etc.

Some method of getting food and water into the cages without opening the doors is advised. A cut section in the bars which can be unlocked and revolved on a central axis is one possibility. It can be reversed, a food pail and water pail put in place with locking rings fastened around them, and then revolved back into position and locked. Thus safe feeding is possible.

Den boxes should be provided. These can be surprisingly small. Boxes $48 \times 36 \times 30$ inches have been used for exceptionally large bears. They may be built of 2×6 inch lumber, insulated, and the insides covered with exploded metal lath or punched sheet steel. The doors can be only 16×16 inches, and the small size is a safety factor when one must work in the cages. Straw should be provided for nesting.

Such dens have been made airtight, except for the door and two 2 inch pipe openings. The entire box was covered with welded seam sheet steel. The door was provided with a flange and rubber gasket, plus a heavy latch. When closed, a pump was started and air flowed in one pipe and out the other to a hose line, and metabolic rate could thus be determined (Hock, 1960b). Thermocouple leads entered the box, so ambient temperature could be constantly monitored.

Bears can be prodigious eaters, but are usually so only in late summer. Furthermore, they seem to tire quickly of foods which may be inexpensive and easy to prepare. Dry dog food may be mixed and fed. The kibbled variety with several flavors is most relished. Canned dog food can be fed occasionally, but bears quickly tire of it. Great success has been achieved with a cooked mix, made as follows: 1000 gm corn meal, cooked in a broth made by stewing bones, meat scraps, fish heads, etc; 2000 gm meat or fish; 250 gm powdered skim milk; 400 gm sugar. The corn meal and meat are cooked together, and the milk and sugar stirred in. It will feed 2 bears for 1 day, except in late summer to early fall, when it may not be enough for 1 bear. It supplies about 450 calories per 100 gm. Apples and other delicacies may be offered. Large amounts of water should always be provided.

Bears usually enter the dens in late fall to early winter. However, not all bears will do so, and few will do so spontaneously. If the bears have fattened properly, food may be removed at the advent of cold weather, say during November. This means *all* food, for even occasionally presenting an apple or sugar cube may prevent the bears from becoming lethargic. After any bear has retired to its den, feeding and watering of all bears must be stopped. In fact, nearly any disturbance will bring them out of the dens. If the doors to the den boxes are closed, care must be taken to see that adequate air is introduced into the dens (20 liters per minute or more), and that water vapor from the exhaled breath does not clog the air hose.

Bears cannot be trusted during their lethargic period, and one must be careful not to touch them, for they are constantly ready to injure one. The "big teddy-bear" appearance of the bear in summer (when they are also not to be trusted!) disappears in cold weather, and they are most treacherous when they are most interesting from the present point of view.

X. Techniques for Use of Hibernators

In general, application of any specific research technique to the study of hibernators should be possible. However, there are some special

features that require recognition if the project is to be successful, and more important, if the results are really to relate to hibernation.

A. General Remarks

It seems absurd to say that the first rule in working with animals in hibernation is to be sure that they are hibernating. However, this is a necessary precaution. Many stimuli will cause an animal in deep hibernation to start to arouse. For example, when an animal is picked up, it will usually start to arouse, and although it may be many minutes before there are any external signs of this, there may be nearly immediate internal differences between the deeply hibernating state and that typifying arousal. For this reason it is essential that all steps in the technique to be applied are well thought out and practiced, and that all manipulations be done with the utmost speed. And, of course, the less disturbance possible the better, especially before the measurement or sample is taken. Some of the techniques referred to in the following sections give specific illustrations of ways to avoid disturbances. Use of these, or similar techniques, will give benefits in reliability and duplicability of data.

One may wish to compare different phases of the hibernation cycle. That is, animals in deep hibernation, in a less profound state, or in a transitional phase may be studied comparatively. The easiest and surest method of determining which of these phases an animal represents is to determine its rectal temperature. This should always be done in concert with any other determination. It may be done just after or during the manipulation, depending on the length of time involved. Caution should be exercised that this is a meaningful measurement, taken deeply if it is a colonic temperature. Methods will be discussed in the next section.

Some experience will be needed to tell if a given subject is deeply hibernating, or just in a deep sleep, or in the process of entering or arousing from hibernation. This is even more essential if one of the lighter states is involved. Furthermore, it often becomes important to know how long the animal has been in deep hibernation for a particular determination. To this end, some sort of "indicator" is needed. Oatmeal flakes may be scattered on the dorsal surface of an animal after it has just entered hibernation. If it arouses, these are shaken off. Pengelley and Fisher (1957) used a larger amount of sawdust, and this is a better method. It should be stressed that daily observation without some system such as this is not adequate, as the animals may arouse and reenter hibernation in a few hours.

It is best to keep the animals in the cold room while they are being worked on, especially if any lengthy process is involved. Care must be taken not to disturb the other hibernators, however, and often one consideration must be balanced against the other.

The following sections are intended to provide potential investigators with authoritative references to work already performed in the several fields of study to be discussed. This is preferable to attempting to digest and spew forth comments on technique in which pertinent points may be naively overlooked. In addition, no attempt will be made to review the "state of the art" in these fields, but reference will be made to the articles cited or to the reviews referred to above.

B. Temperature Determination, Temperature Regulation

Determination of the body temperature of animals during hibernation is the commonest measurement performed, and lowered body temperature may be regarded as one of the definitive aspects of this condition. Although the body temperature itself may not be the determination under primary study, it should always be taken along with other parameters.

Lyman (1948) inserted indwelling thermocouples in the cheek pouches of hamsters. Lyman and Chatfield (1950) describe thermocouples for temporary insertion into soft tissues. Other methods have been used by other workers, including my subdermal abdominal thermocouple for bats (Hock, 1951), but no one has successfully utilized an indwelling rectal probe, as the animal will not tolerate it when active or hibernate with it in place. Folk (1962) has utilized implanted radiotelemeters, and this method seems to promise great success.

Small mammals such as bats exhibit low tissue temperature gradients when they are in deep hibernation. Thus core and peripheral temperatures approximate each other, and temperature measurements made in areas other than the body's core are more indicative of deep body temperatures than is ordinarily true. Lyman and Chatfield's (1950) work indicates that this is not true after disturbance leading to arousal, and Lyman (1958a) shows that it is not true during entrance into hibernation. At the onset of hibernation he found the heart of the woodchuck is the warmest part of the body, and it remains 1°C or more warmer than other parts of the body until the animal reaches the temperature of deep hibernation, when these differences in body temperature decrease. In small animals, such as the bat and the hamster, where thermal gradients during deep hibernation are low, there is little difference between the anterior and posterior body temperatures. Several workers (Lyman and

Chatfield, 1950; Lyman, 1948; Lyman and Taylor, 1964; R. E. Smith and Hock, 1963; Smalley and Dryer, 1963) have demonstrated the nonuniform distribution of body heat which occurs during arousal. In all animals studied the anterior portion of the body warms more rapidly than the posterior portion, and in most cases the heart is the warmest part of the body [see R. E. Smith and Hock (1963) for an exception].

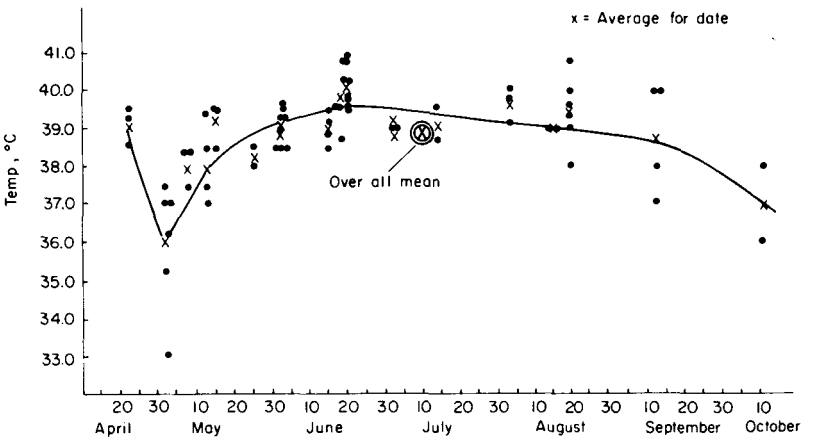

FIG. 7. Mean colonic temperature of wild Arctic ground squirrels throughout the active season. Reprinted, with permission, from Hock (1960a).

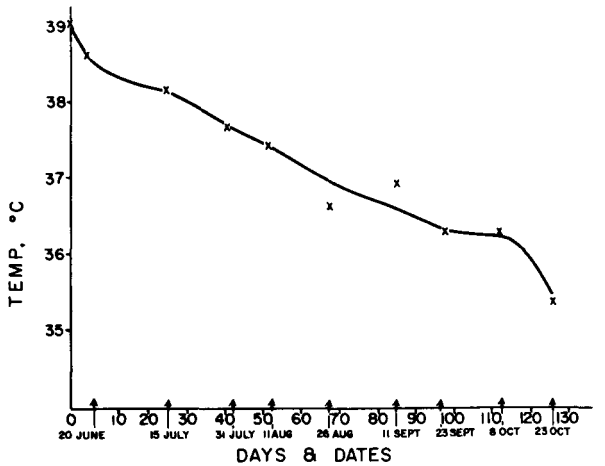

FIG. 8. Mean colonic temperatures of captive Arctic ground squirrels in summer. Reprinted, with permission, from Hock (1960a).

Caution must be exercised in the comparison of hibernating body temperatures with those of the active state. Hock (1956) studied rectal temperature variations in wild Arctic ground squirrels while they were active. A high temperature (39°C) is found in early summer, in contrast to lower temperatures just following emergence from hibernation and just preceding entrance into hibernation (Fig. 7). Hock (1960b) compared this seasonal cycle with rectal temperatures of captive Arctic ground squirrels, in which a continual decline occurred as a function of time in captivity, with a greater decrease preceding entrance into hibernation (Fig. 8).

Strumwasser (1959a, b, c,) used implanted cortical electrodes to determine brain temperatures during deep hibernation and entrance into that condition. Other studies relating to some aspect of temperature regulation include those of Farrand (1959), Herreid (1963a,c), Gelineo (1938a,b, 1939), Gelineo and Sokic (1953a,b), and Kayser (1940).

C. Metabolism and Respiration

Respiratory rate can be determined by eye only with difficulty during hibernation, for respirations are feeble, irregularly timed, and interspersed with bouts of Cheyne-Stokes breathing. Plethysmographs can be used, but Battista and Dawe (1959) describe a simple automatic device for this measurement. The work of Landau and Dawe (1958) was done with this instrument.

Many studies have been made on whole-body metabolic rate, using a number of different methods. Among these are: bats (Hock, 1951; Pohl, 1961; Herreid, 1963a,b); jumping mice (Morrison and Ryser, 1962); hamsters (Lyman, 1948; Kayser, 1952c, 1959a); ground squirrels (Hock, 1960a,b; Kayser, 1952b); marmots (Lyman, 1958a); dormice (Kayser, 1959a; Kayser *et al.*, 1958); and kangaroo mice (Bartholomew and MacMillen, 1961). Some general remarks on this phenomenon have been made by Kayser (1950a,b, 1957a), Lyman (1958b), and V. Popovic (1957).

The method used for determination of the metabolic rate of the black bear during its lethargic period (Hock, 1960b) is described in Section IX, J. In addition, a method for long-term MR determinations of Arctic ground squirrels has been used, wherein the squirrels live in large glass desiccators. The investigator can then connect the desired desiccator to the airline, and monitor oxygen consumption by paramagnetic means, and carbon dioxide production by infrared determination.

A multiple chamber, closed circuit apparatus used for metabolic determinations on bats is described elsewhere (Hock, 1953).

D. Biochemical and Cellular Studies

A variety of histochemical and biochemical studies have been made on the tissues of hibernators including the periods of entrance into and arousal from hibernation, as well as the period of deep hibernation itself.

The effect of hibernation on the catecholamine content of extra-adrenal tissue has been studied by Musacchia *et al.* (1962) in the 13-lined ground squirrel, and by Uuspää (1963a) in the hedgehog. Uuspää (1963b) has also studied the catecholamine content of the hedgehog adrenal gland.

Zimny and co-workers have studied the effects of both long- and short-term hibernation on phosphate compounds in liver, heart, and skeletal muscle of the 13-lined ground squirrel (Zimny, 1956; Zimny and Gregory, 1958, 1959). It is of interest that although both the adenosine triphosphate (ATP) and phosphocreatine (PC) content of cardiac muscle decrease during hibernation, the ATP/PC ratio is at its maximum, indicating that the ATP level is maintained at the expense of phosphocreatine and is therefore a readily available source of energy for the slowly beating heart. Kristoffersson (1961) has examined ATP and orthophosphate levels in several tissues of the European hedgehog and has compared his findings with those of previous workers. Zimny (1956) also studied the lactate content of heart and skeletal muscle of the ground squirrel and Hanson and Johansson (1961) studied this compound in the hedgehog.

It appears evident that fat is the main source of energy during hibernation, and glycogen is the main source during arousal (Lyman and Chatfield, 1955). It is, therefore, not surprising that considerable work has been done on the effect of hibernation and arousal on the distribution of these compounds as well as their precursors and breakdown products. Zimny (1956) studied glycogen depletion during long- and short-term hibernation in the 13-lined ground squirrel. Lyman and Leduc (1953) found liver and muscle glycogen in hibernating hamsters to be similar to that of awake animals, whereas the cardiac glycogen was increased during hibernation. During arousal in the hamster (Lyman and Leduc, 1953) liver, muscle, and cardiac glycogen all decrease; this drop is most rapid and pronounced during the second hour or later of arousal, at a time when the body temperature is rising rapidly. In the 13-lined ground squirrel (Zimny and Gregory, 1958) there is a decrease in glycogen of liver, heart, and skeletal muscle during the early stages of arousal, but in the later stages, tissue glycogen levels increase, probably indicating glyconeogenesis. Mayer and Bernick (1957)

did a histochemical study of the distribution of glycogen, lipids, and amino acids in the liver, heart, and tongue of the Arctic ground squirrel. Hannon and Vaughn (1961), using biochemical methods, found a two-fold increase in skeletal as well as cardiac muscle glycogen and no change in liver glycogen in the Arctic ground squirrel during hibernation. Musacchia and Wilber (1952) examined the lipid content of kidney and liver of the Arctic ground squirrel and found that it gradually decreases during hibernation, indicating that fat turnover probably supplies energy during this period. Troyer (1959) and Leonard and Wimsatt (1959) have examined glycogen levels in bats. Both studies showed a sharp drop (up to 50%) in liver glycogen during arousal. Both glycogen and lipid levels in the liver of the marmot have been studied by Weill and Kayser (1957).

Recently, C^{14}-labeled acetate has been used to study metabolic pathways in hibernators. Rebel *et al.* (1960) studied its incorporation into fatty acids and glycogen in several tissues of the ground squirrel, *Citellus citellus*. As a result of this study they concluded that brown fat and heart synthesize glycogen during hibernation and fatty acids when the animal is active. Using this isotope, Denyes and Carter (1961a) showed a decrease in hepatic lipogenesis in the hamster during hibernation, and Baumber and Denyes (1963) found an increase in $C^{14}O_2$ production in epididymal fat.

Tissue respiration studies have been made by a number of workers. Pantesco *et al.* (1961) measured oxygen consumption and glycolysis in slices of cerebral cortex, myocardium, and kidney of the European hamster and compared these with similar measurements from the rat. Bidet *et al.* (1962) measured oxygen consumption and ATP formation in homogenates of brain and heart from two hibernators (European hamster and European ground squirrel), and compared these with similar measurements from rat and guinea pig. Hannon *et al.* (1961) studied the *in vitro* endogenous tissue respiration of cerebral cortex, liver, myocardial, and skeletal muscle homogenates from the Arctic ground squirrel and found that, when measured at 38°C, all these tissues showed a reduction in endogenous respiration. Denyes and Hasset (1960) studied the endogenous respiration and substrate utilization of liver, kidney, and diaphragm slice from hamster.

The effect of temperature on *in vitro* tissue respiration has been studied by Kayser *et al.* (1954) using kidney slice from hamster and ground squirrel. They have shown that tissue from these animals differs significantly in its response to temperature from kidney of nonhibernators. Hook and Barron (1941) measured the respiration of kidney and brown fat slice from the 13-lined ground squirrel at the temperatures of hiberna-

tion (8°C) and activity (38°C). South has done considerable work on the effect of temperature on tissues from hibernators. Among the measurements he has made are: oxygen consumption and glycolysis of brain and heart slice from hamster, bat, and rat (South, 1958); electrical and mechanical properties of phrenic nerve-diaphragm preparations from hamster and rat (South, 1961); and oxidative phosphorylation of heart mitochondria from hamster (South, 1960). He has used a temperature range from 5°C to 38°C or 43°C for most of these studies and has calculated energies of activation (E_a) for the processes examined. In general he finds that in nonhibernators these E_a values are higher than those found in the hibernators with which they were compared. Meyer and Morrison (1960) measured respiration of a number of tissues from the 13-lined ground squirrel.

A few enzyme studies have been made on the tissues of hibernators. Leonard and Wimsatt (1959) found that phosphorylase levels of skeletal muscle and liver of bats were higher after arousal than during hibernation. Zimny and Bourgeois (1960), using histochemical methods, studied the distribution of enzymes in the kidney of the 13-lined ground squirrel and concluded that this distribution did not change during hibernation. Chaffee *et al.* (1960, 1963) examined liver and kidney enzymes of the hamster during prehibernation cold-exposure and found that 3 of the 4 enzymes examined increased in activity during this period. They suggest that intracellular enzymatic adjustments may in part account for the necessity on the part of the hamster to cold-acclimate before hibernation. Hannon and Vaughn (1961) measured the activities of enzymes associated with glucose metabolism in the liver and heart of the Arctic ground squirrel. They compared these enzyme activities with those from the rat, discussing the differences between hibernator and nonhibernator. As a result of these studies they postulate probable mechanisms and pathways of glucose and glycogen metabolism during hibernation. Chaffee *et al.* (1961) have examined oxidative enzymes and phosphate esterification in liver mitochondria from the hamster. When measured at 7°C *in vitro,* succinic and glutamic oxidase activities are markedly reduced from the 37°C level. Chaffee (1962) has made further studies of succinoxidase and postulates an inhibitor of this enzyme which operates at 7°C during hibernation, but which is inactive at 37°C.

E. Heart and Circulation

One of the more obvious distinctions between hibernators and nonhibernators is the continuance of the heart beat at very low body temperatures, without the intervention of ventricular fibrillation. Lyman and

Blinks (1959) studied isolated perfused hearts of a number of rodent species, and found that in nonhibernators the heart ceased to beat at about 10–15°C. Hibernator's hearts, however, maintained beat until chilled to 7°C to −1°C, depending on the species. Michael and Menaker (1963) have extended identical studies to the heart of the bat, *Myotis lucifugus*, and found the rate-temperature curve to fit the Arrhenius equation, and to have a Q_{10} of 3.5.

Covino and Hannon (1959) compared Arctic ground squirrel and rabbit hearts. Below 25°C the rabbit heart was more susceptible to cold, and at 15°C exhibited differences in ATP-ADP (adenosine diphosphate) conversion, ventricular nucleotide content, and glutamic, β-hydroxybutyric, malic, and succinic oxidase activities.

Hirvonen (1956) found that isolated auricles of the hedgehog and hamster continued to beat at 1.5–6°C, whereas rats' auricles ceased at 16–18°C. Heat standstill occurred thus: hedgehog, 37–40°C; hamster, 46.6°C; rat, 48.7°C. Marshall and Willis (1962) studied membrane potentials in isolated atria of *Citellus tridecimlineatus*. Action potentials increased in height and in duration at 15°C and 6°C, but not as a result of the slower beat. These authors suggest that the observed increases in amplitude and duration increase the ability of the action potential to propagate excitation at low temperature.

Electrocardiographic (EKG) studies by Dawe and Morrison (1955) were performed on hedgehog, and Arctic and Franklin ground squirrels. They found heart rates as low as 2.2 beats/minute. Electrocardiographic components were all "stretched" at these low temperatures, especially the T-P interval. Thus the SA node's automaticity is most slowed in hibernation. Additional EKG studies include those by Nardone (1955) on the Arctic ground squirrel, Sarajas (1954) for the hibernating hedgehog, and Johansson (1957a) on the nonhibernating hedgehog. The last author also studied badgers (1957a), and found cessation of the heartbeat at 14°C, typical of nonhibernating mammals. Kayser (1957b) has discussed critical thermal increments for events in the EKG of the European hamster and *Citellus citellus*. Hiebel and Kayser (1950) studied the EKG during arousal from hibernation.

Biörck *et al.* (1956a) found that administration of pure N_2 for 2 hours altered the shape of the EKG of the hibernating hedgehog. Johansson (1963) could not produce ventricular fibrillation in hedgehogs, hibernating or nonhibernating, by administration of aconitine, adrenaline, or procaine.

Lyman (1958b) found decrease in heart rate to presage the entrance into hibernation, preceding a drop in either body temperature or oxygen consumption. Suomalainen and Sarajas (1951) found the heart rate of

the hibernating hedgehog to be 10% or less that of the nonhibernating level. Lyman (1951) found 13-lined ground squirrels to show an increase in respiration and heart rate when exposed to CO_2 concentrations of 2.5%, but to remain in deep hibernation. Hamsters required 5% CO_2 to increase heart rate, and would arouse.

Dawe and Landau (1960) have ably discussed the heart of the hibernator in hibernation, during arousal, and during entrance into hibernation. Thirteen-lined ground squirrels were used for test animals, but the discussion should be read by anyone studying the heart in hibernation.

Chatfield and Lyman (1950) pointed out the differential vasoconstriction between fore and hind parts of the body that occurs during arousal from hibernation. Bullard and Funkhouser (1962) further demonstrated, by use of Rb^{86}, an initial confinement of blood flow to the thoracic region until the heart rate reaches 100 beats/minute. Flow then increases to anterior portions of the animals, and even at 200 beats/minute posterior flow is still low. Soivio (1963), using induced hypothermia in hedgehogs, found much the same picture. McBirnie *et al.* (1953) found peripheral circulation of woodchucks to be maintained at 5°C without intravascular agglutination or stasis.

Lyman and O'Brien (1963) discuss the sympathetic control of circulation in the hibernating cycle of ground squirrels. Chronically implanted aortic cannulae were utilized to infuse drugs into the blood, as described by V. and P. Popovic (1960) and V. Popovic *et al.* (1963). Using the same technique, Lyman and O'Brien (1960) measured blood pressure throughout the cycle of hibernation. Mean blood pressures averaged 119 mm before hibernation, with a drop to 40–90 mm in systole and 7–40 mm in diastole during hibernation.

F. Hematology

There are a number of studies on classic hematological changes associated with hibernation. Red and white cell counts have been made by Suomalainen and Granström (1955) and Lyman *et al.* (1957) for the hamster; by Stuckey and Coco (1942) for the 13-lined ground squirrel; by Rasmussen (1916) for the woodchuck; by Biörck *et al.* (1956b) for the hedgehog; and by Svihla *et al.* (1955) for the black bear. Riedesel (1957) has summarized many of these studies, and further discussion of cell counts, hemoglobin, and hematocrit may be found in the various reviews cited earlier, as well as in the papers mentioned above.

Blood sugar has been found by Lyman and Leduc (1953) to be higher in hibernating hamsters than in nonhibernating ones, a situation in contrast to that found by other authors in other species. Dodgen and Blood

(1953) and Raths (1961) have discussed the blood sugar and its energy aspects in the bat and European hamster, respectively.

Blood and plasma volumes have been studied by Svihla and Bowman (1955) in the hamster, and by Kallen (1960a,b) in the little brown bat. Brock (1960a) has found an extension of erythrocyte life from 40 days in active hamsters to 160 days in hibernating ones, with a concomitant low rate of erythropoiesis during hibernation. Lyman *et al.* (1957) found that the reticulocyte response which occurs after massive hemorrhage in active hamsters is suppressed in animals bled during hibernation and occurs only after the termination of hibernation. This paper contains a good review of the changes in blood and hematopoietic organs during hibernation.

Blood gas studies have been done by McBirnie *et al.* (1953) on the woodchuck, by Svihla and Bowman (1952) on the Arctic ground squirrel, and by Lyman and Hastings (1951) on hamsters and ground squirrels. Although the picture with respect to blood pCO_2 varies from species to species, in general these workers have found that during hibernation the oxygen content, red blood cell concentration, and therefore the oxygen-carrying capacity of whole blood are increased, thereby tending to prevent tissue hypoxia which might otherwise result from the reduced cardiac and respiratory activity found during hibernation.

Suomalainen and Karppanen (1956, 1961) have studied serum protein changes in the hedgehog and found that, in hibernation, the total protein increases as a result of an increase in the albumin fraction, whereas the globulin content does not change significantly. In the hamster, South and Jeffay (1958) found an increase in total serum protein, albumin, and β-globulin and a decrease in α-globulin during hibernation. Upon arousal, the serum protein levels returned to those of the nonhibernating controls.

There are many studies on electrolyte levels in hibernation. Riedesel and Folk (1958) have given data on several species. Both Suomalainen (1939) and Riedesel (1957) have discussed the effect of serum magnesium on hibernation. Raths (1962) has summarized his studies on the changes in serum sodium, calcium, and potassium in the European hamster during the phases of the hibernation cycle and compared these with serum electrolyte changes found during artificial hypothermia. Kristoffersson (1961) discussed ATP and orthophosphate levels in the blood of hedgehogs, and Brock (1960b) studied blood phosphate changes in hamsters.

The blood of mammals in hibernation does not clot readily (Svihla *et al.*, 1951, 1952a; D. E. Smith *et al.*, 1954a,b; Suomalainen and Lehto, 1952; Denyes and Carter, 1961b). Svihla *et al.* (1952b) found a reduced prothrombin and therefore an increased clotting time in dormant ground

squirrels whether estivating or hibernating. Härma and Suomalainen (1951) found an increased number of heparinocytes, or mast cells, in the intestine and lungs of the hibernating hedgehog and interpreted this to indicate an increase in heparin secretion during hibernation. The finding was confirmed in *Myotis lucifugus* by a similar increase in mast cells (D. E. Smith *et al.*, 1954b). Biörck *et al.* (1962) have discussed reduction of prothrombin in hedgehogs, and Lechler and Penick (1963) have made a general study of the blood clotting mechanism in the 13-lined ground squirrel. Bragdon (1954) has discussed hyperlipemia and accompanying atheromatosis in the Columbian ground squirrel.

G. Nervous System

One of the chief distinctions between hibernators and homoiothermic mammals is the maintenance of irritability of the former when the body (or brain) temperature is greatly reduced. Kayser and Richert (1958) have shown arrest of cortical electrical activity in the rat at 18.4°C rectal temperature, whereas European ground squirrels and European hamsters still show cortical discharges at about 5°C. Kayser *et al.* (1951) observed absence of spontaneous cortical activity at 5°C brain temperature in *Citellus citellus,* but Kayser (1961a) later observed that spontaneous activity occurred at 6°C early in the experiments, and could be elicited by handclap stimuli until 3 hours had elapsed, whence cortical silence was maintained for up to 5 hours. Lyman and Chatfield (1953) found that the woodchuck showed spontaneous cortical activity as low as 6°C.

Chatfield *et al.* (1951) studied the golden hamster, and found that cortical activity during arousal commenced at 19–21°C. However, peripheral movement could be caused by electrical stimulation of motor areas at temperatures down to 12°C. Thus it appears that the hibernating hamster is functionally decorticate. However, other parts of the nervous system apparently retain their function at low temperatures in order to mediate the arousal reaction. Among the necessary neural components would be the peripheral nerves, the subcortical heat regulating centers, presumably in the hypothalamus, and the associated sensory and motor systems. Chatfield and Lyman (1954) also studied subcortical actvity in the golden hamster during arousal. At temperatures between 5.5°C and 16°C, they found that spontaneous electrical activity was confined to the components of the limbic system and that the mechanical stimulus of handling probably caused activity in these structures. They therefore concluded that arousal in the hamster is initiated when peripheral afferent impulses stimulate the limbic system.

Nerve conduction during hibernation has been studied by Chatfield

et al. (1948), using golden hamsters. Cessation of function did not occur until the temperature decreased to 3.4°C, whereas rat nerves ceased conducting at 9°C. Kahana *et al.* (1950) measured the electrical responses from the round window of the ear of the golden hamster and found that the auditory nerve ceased conducting impulses below 18°C, thus showing functional deafness.

Strumwasser (1959a, 1960) found that in *Citellus beecheyi* focusing of attention, discrimination, localization of sound, vocalization, and motor coordinations all were possible at brain temperatures of 6.1°C. A 90% reduction of amplitude of brain wave activity was found at this brain temperature.

Azzali (1952), Suomalainen and Nyholm (1956), and Suomalainen (1960) have studied neurosecretion in the hedgehog and find that it is increased during hibernation. Kayser and Malan (1963) have reviewed the role of the central nervous system in hibernation, and those interested in this facet of hibernation are referred to this paper and the references therein.

H. Endocrines

The role of the endocrine system is most evident during the preparatory period which precedes hibernation, at which time a general involution of all the endocrine glands occurs. No single hormone has been shown to play the decisive role in controlling hibernation, nor have extirpation experiments shown that any one gland "controlled" hibernation. However, the adrenal cortex is required in order for hibernation to occur. In adrenalectomized animals, injections of cortisone and deoxycorticosterone restore the ability to hibernate (V. Popovic, 1960a). Similarly, Kayser and Petrovic (1962) showed that grafts of adrenal gland from young hamsters into adrenalectomized adults restored the ability of the adult to hibernate.

This field has recently been extensively reviewed by Popovic (1960a), and reference should be made to this paper and its bibliography.

Brief mention should be made here of recent papers not considered by Popovic. Histological studies of endocrine glands include those of Zimny (1959) on the adrenal gland of the 13-lined ground squirrel; by Mayer and Bernick (1959) on the thyroid, adrenals, hypophysis, and islets of Langerhans of the Arctic ground squirrel; by Kayser *et al.* (1961) on the parathyroid of the European hamster; and by Hoffman and Zarrow (1958a) on the pituitary of the 13-lined ground squirrel.

Egdahl and Richards (1955) studied adrenal cortical function in the black bear under artificial cooling. Denyes and Horwood (1960) studied

adrenal cortical steroid levels in the hamster, and Raths and Schulze (1957) studied the adrenal of the European hamster, during both activity and hibernation. The thyroid has been studied by Lachiver and Petrovic (1960) in the dormouse *Eliomys quercinus*, by Kayser *et al.* (1959) in the European hamster, by Kayser and Aron (1952) and Lachiver and Petrovic (1960) in the European ground squirrel, by Hoffman and Zarrow (1958b) in the 13-lined ground squirrel, and by Sadler and Tyler (1960a,b) in bats. The last papers are the product of the recent upsurge of interest in bat rabies in the United States. Suomalainen and Saure (1955) have studied the islets of Langerhans of the hedgehog, and Portius and Raths (1957) have examined their activity in both hibernating and active golden hamsters.

I. Kidney, Water Balance

The study of kidney function and water balance in hibernators has until recently been much neglected. Since most mammals in hibernation are metabolizing fat and thus deriving metabolic water, the problem of water balance may well be minimal or even nonexistent in these animals. Still, as Kayser (1961a) has pointed out, small-sized hibernators do have a water loss problem, and his book should be referred to for a discussion of this (p. 60). During hibernation in the wild, most hibernators are found in small underground chambers, presumably in a near-saturated atmosphere. Thus, studies made on caged animals in cold rooms may show vast differences in evaporation and general water loss. A method such as that described above (see Section IX, D) for housing animals in dessicator jars may be helpful in maintaining more nearly natural conditions with respect to atmospheric water vapor.

Svihla (1941) thought that dehydration was responsible for estivation, and that, conversely, intraperitoneal injections of water could cause arousal. He and his colleagues (Svihla *et al.*, 1953) further tested this hypothesis on ground squirrels by injecting not only water but the inert substance, mineral oil. In both studies they found water injections caused arousal, while in the latter study mineral oil injections did not. In spite of these observations it seems likely that in many cases the injection itself might easily cause arousal or that the additional water might upset an otherwise "normal" water balance, to say nothing of the pain involved in water injection.

The kidney of hibernators has been examined histologically by Engel *et al.* (1957), who studied changes in the zona glomerulosa during activity, hibernation, and after arousal in the European and golden

hamsters. Zimny and Bourgeois (1960) examined the kidney of the 13-lined ground squirrel, *Citellus tridecimlineatus*, and found that during hibernation there was a pronounced vasocongestion of the glomeruli and vasa rectae. Chaffee and Cunningham (1962) and Chaffee *et al.* (1963) have found a marked increase in kidney size in cold-exposed hamsters, although these animals were not hibernating. Shortly after cold-exposure there is an increase in mitotic activity, especially in the proximal tubule. After 8 weeks in the cold, this mitotic activity has ceased and the kidneys of these animals resemble those of a renal hypertensive rat.

Zimny and Bourgeois (1960) have shown that the composition of the urine of the 13-lined ground squirrel changes during hibernation. There are marked increases in glucose and potassium concentrations, a marked decrease in sodium, and smaller decreases in chloride and urea concentrations.

Hong (1957) has studied kidney function during hypothermia and hibernation in the 13-lined ground squirrel. He has found that, in hibernation, urine flow is markedly reduced and the urine formed is dilute. The majority of his experiments were done on animals made artificially hypothermic, but it appears that they can be extrapolated to include animals in hibernation. During hypothermia he found that renal blood flow and urine flow decreased, the pH of the urine decreased as did the chloride concentration, while the concentration of reducing substances such as glucose increased. As a result of these and other observations, Hong concluded that both the reabsorptive and secretory functions of the kidney tubule are depressed during hypothermia, and that the reduced urine flow may be due mainly to a decreased glomerular filtration rate resulting from a decreased renal blood flow. If urea injections into ground squirrels are followed immediately by hypothermia, there is no increase in urine urea concentration, indicating an apparent inability of the kidney to concentrate this substance during hypothermia. This may help to account for the high blood and tissue levels of urea found by Kristoffersson (1963) in the hibernating hedgehog.

J. Digestive Tract

As is true for the previous section, little has been written on digestion of hibernators. Since food is usually not present in the digestive tract during hibernation (although it is present at times), the process of digestion is of less interest than the metabolism of foodstuff from the fat depots.

Kayser (1961a) has reviewed the available literature on digestive se-

cretion, and reference should be made to his book. Mayer and Bernick (1957, 1958) have made histological and histochemical studies of the digestive tract of the Arctic ground squirrel. The histological changes in the tract during hibernation are those which would normally be expected to occur in an animal which is not ingesting food. There is an increase in the secretion and storage of mucous material in the cells of the superficial epithelium and it is possible that this increased mucus prevents adhesions between the walls of the collapsed gut during hibernation or prevents autodigestion of the mucosa by enzymes and acid remaining in the stomach (Mayer and Bernick, 1958). Musacchia and Neff (1963) studied *in vitro* absorption of D-glucose by intestinal segments of the 13-lined ground squirrel. Thomson *et al.* (1962) examined liver regeneration in the same species and found that even during hibernation some regeneration took place.

K. Reproduction

It is obvious that animals which spend 6–8 months of the year in withdrawal from the strains and vicissitudes of life, must compress all their activities into the time remaining. This is especially true of reproduction, for as I have pointed out in reviewing the compressed breeding activities of the Arctic ground squirrel (Hock, 1960b), the young of the year must be allowed time to accumulate adequate fat reserves so that they may enter hibernation in the fall.

The 13-lined ground squirrel is the hibernator which has been studied most extensively in this respect. Johnson *et al.* (1933) studied its sexual cycle in the laboratory. Johnson and Wade (1931) made manipulations involving pituitary implants, ovarian implants and injections, and ultraviolet light without inducing breeding. Wells (1935) and Moore *et al.* (1934) studied factors controlling the reproductive organs of ground squirrels. Wells and Zalesky (1940) found that if these animals were maintained at 4°C, they could be kept in reproductive condition throughout the year. Injections of the gonadotropin, antuitrin-S, into male ground squirrels caused testicular activity (Baker and Johnson, 1936).

Wimsatt (1942, 1944) showed that sperm remained viable from the time of insemination of female *Myotis lucifugus* in the fall until the resumption of activity in the spring, at which time ovulation and fertilization occurred.

Johnson (1931b) described the early post-natal life of the 13-lined ground squirrel. Mayer and Roche (1954) and Shaw (1925b) have dealt with this subject in the Arctic and Columbian ground squirrels, respectively.

L. Fat Deposition, Brown Fat

Most animals that hibernate become extremely fat before hibernation and apparently live off this stored fat during hibernation. Wade (1948) has described rapid fat deposition in the ground squirrel prior to hibernation, and the hedgehog is said to depend entirely on its fat stores during hibernation (Lyman and Chatfield, 1955). The golden hamster appears to be an exception to the above rule (Lyman, 1954) for it stores large quantities of food prior to hibernation and, although it increases its food and water intake upon exposure to cold, it does not become extremely fat and may even be quite lean when it hibernates. Fawcett and Lyman (1954) have examined the depot fat of hamsters and ground squirrels. In the hamster they found that cold exposure resulted in an increase in the iodine number of depot fat from 83.7 to 87.3, indicating a decrease in saturation of the fat and a decrease in melting point. The iodine number of the ground squirrel's depot fat is higher than that of the hamster (93.5), and because this animal enters hibernation rapidly upon exposure to cold no change in the iodine number could be measured. Based on melting point measurements, the degree of unsaturation found in the body fat of these animals would indicate that their fat remains in a liquid or semiliquid state even at the temperature of hibernation.

Aside from white fat, all true hibernators and several nonhibernators possess another type of fat—brown fat (Johansson, 1959). This was first described by Gesner in 1551 and differs from white fat in being multilocular, brown in color, having a spherical, more or less centrally located nucleus, a rich blood and nerve supply, and a high *in vitro* respiratory rate. Its morphology, general locations, distribution, and possible functions have been reviewed by Rasmussen (1923), and more recently by Boerner-Patzelt (1957) and Johansson (1959). The main mass of this tissue is located anteriorly in the body in the interscapular, cervical, thoracic, and axillary regions (Rasmussen, 1923). It is the interscapular mass which is commonly referred to as the "hibernating gland," a name first given to this structure by Barkow in 1846.

The chemical composition and enzyme content of brown fat have been studied by a number of workers. Fawcett (1952) has examined various lipids, enzymes, and glycogen in both brown and white fat of rats and mice and found that, except for neutral fats, these compounds are all more abundant in brown fat. Remillard (1958) studied the annual variations in the lipids of bat interscapular brown fat. Chaffee and Smith (1963) have studied the effects of heat and cold on oxidative enzymes in hamster brown fat. George and Eapen (1959a,b) have examined lipase, succinic dehydrogenase, and lactic dehydrogenase in brown and

yellow (i.e., depot) fat of bats. Brown fat has been shown to contain all the enzymes necessary for the synthesis and breakdown of glycogen (Mirski, 1942; Shapiro and Wertheimer, 1956). Joel and Ball (1962) have reported a high cytochrome content in the brown fat of rats, as high as that of any other tissue. These authors feel this high cytochrome content accounts for the characteristic brown color of this tissue. It also correlates with the high respiratory rate found by Hook and Barron (1941) in brown fat of the 13-lined ground squirrel, and by George and Eapen (1960) for the brown fat of the bat.

The possible function or functions of brown adipose tissue has been the subject of considerable experimentation. Brown fat has often been considered to function as a storage organ (Rasmussen, 1923). Langer and Langer-Schierer (1959) and Langer-Schierer and Langer (1957) believe it functions in this capacity in the hamster and rat, storing lipids, glycogen, and proteins. Weill *et al.* (1957) considered the brown fat of the marmot to be a reservoir for protein, fat, and carbohydrate.

As early as 1913 Vignes attempted extirpation of the "hibernating gland" of hedgehogs and found its complete removal impossible because of its diffuse nature. In rats, however, where the operation was simpler, he found that "hibernectomy" caused a loss in weight, failure to eat, and finally death. More recently Zirm (1956a) has found that removal of roughly 50% of the total brown fat of the hedghog results in the animal's death upon exposure to extreme cold. (For further references to extirpation experiments, see Johansson, 1959.)

Several workers have attempted to extract a substance from brown fat which, when injected into nonhibernators, will produce effects suggestive of hibernation. Bigelow (1954) tried unsuccessfully to extract a substance from the brown fat of woodchucks that would improve the cold tolerance of nonhibernators. Zirm (1956b, 1957) has extracted a yellow-green substance from the "hibernating gland" of hibernating hedgehogs, which when injected into mice caused a decrease in body temperature, respiratory rate, and blood pressure. Similar extracts of brown fat from active hedgehogs did not produce these effects. Since he could not obtain this substance from other organs of the hibernating hedgehog, Zirm assumed that it was produced in the hibernating gland and that this gland therefore had an endocrine function. Zirm (1956a) has also found that samples of brown fat from hibernating hedgehogs implanted into mice cause a decrease in body temperature and metabolism and a marked increase in body weight. Langer-Schierer and Langer (1957) disagree with Zirm's conclusions. In a histochemical and biochemical study of the brown fat of the hamster and the rat they found that, for the materials studied, no differences could be found

between the hibernating and nonhibernating species. They further concluded that the tissue functioned in the storage of glycogen, lipids, and possibly other substances, but did not appear to have a secretory function. In an attempt to test some of Zirm's observations, Morrison and Allen (1962), using brown fat from ground squirrels, found that neither tissue implants nor injections of homogenate caused a reduction in body temperature in mice. Haberey *et al.* (1960a,b), using Zirm's method, prepared an extract of brown fat from hibernating hedgehogs and found that its injection into rats did not alter their response to artificial cooling. Furthermore, in adrenalectomized rats it had an effect similar to, but less pronounced than cortisone in protecting against hypothermia during cold-exposure.

Suomalainen and Herlevi (1951) have examined sudanophil changes in brown fat of the European hedgehog during arousal and concluded that arousal is such a physiological stress that it induces an alarm reaction in brown fat similar to that found in the adrenal cortex, i.e., a reduction in both size and number of sudanophil particles.

Recent studies (R. E. Smith, 1961; Smith and Roberts, 1964) have shown that in rats exposed to cold brown fat plays an important thermogenic role, increasing both in mass and in unit heat production in response to cold stress. A thermogenic effect of brown fat during arousal from hibernation has been demonstrated both in the yellow-bellied marmot (Smith and Hock, 1963) and the little brown bat (Smalley and Dryer, 1963). These workers have found that during arousal the temperature of the brown fat exceeded that of the other tissues measured. However, in the 13-lined ground squirrel, the heart temperature evidently exceeds that of the brown fat during certain phases of the arousal (Lyman and Taylor, 1964). In the latter species, Joel *et al.* (1964) have shown that during arousal the brown fat loses approximately 1 gm or 50% of its total lipid. If completely oxidized, this is estimated to be more than enough lipid to provide the calories necessary to warm the entire animal from 5°C to 48°C. Anyone who has witnessed arousal from hibernation, however, must also concede the thermogenic role of the muscles in the rewarming process.

M. Cycles, Periodic Arousal

It is obvious that hibernators exhibit profound seasonal variations. I have said (1960b) that the whole year is involved in preparing for hibernation, hibernating, or recovering from that condition. Studies on annual weight variation, body temperature, and metabolic rate in Arctic ground squirrels and black bears have been given as evidence for the above

statement (Hock, 1960b). Other data on these annual cycles may be found in Kayser (1961a).

Folk (1957) and Folk *et al.* (1961) have studied persistence of 24-hour rhythms during hibernation. Folk later (1962) studied heart rate of Arctic ground squirrels by use of implanted radio capsules, but has thus far not made such studies during hibernation.

One of the most interesting phenomena associated with hibernation is the periodic arousal exhibited by all species in which deep hibernation occurs (Fig. 9). This is a great boon to the student of hibernation, for

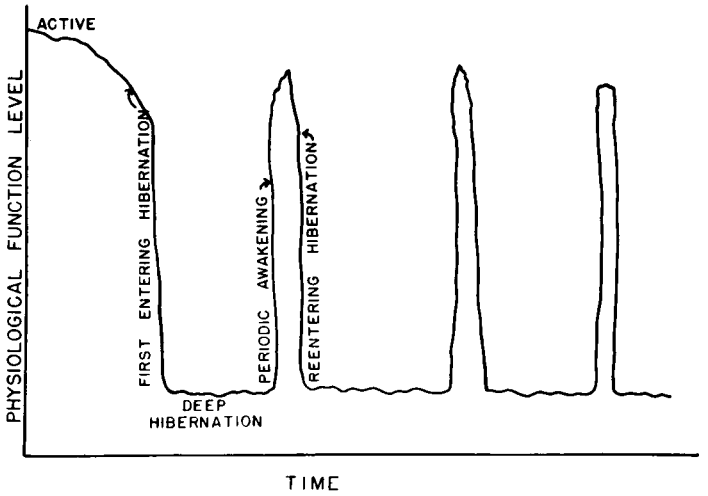

FIG. 9. Concept of hibernation, and periodic arousals. Reprinted, with permission, from Hock (1958a).

instead of a single occurrence of hibernation in a year, there are a number of such "bouts." The number and length of these "bouts" varies for different species, as well as seasonally. Thus the length of a single "bout" of hibernation may be 3–5 days in golden hamsters (Lyman, 1948), up to 16 days in golden-mantled ground squirrels (Pengelley and Fisher, 1963), and up to a month in the marmot (Dubois, 1896).

The process of arousal is dramatic. With its onset the deeply hibernating mammal, such as the Arctic ground squirrel (the species most familiar to the author), spontaneously begins to increase its heart rate, body temperature, respiration, and oxygen consumption. Stimulus for this arousal can be applied by the investigator in the form of light handling. The rate of increase in the above parameters is slow at first, but increases with time. See Lyman (1948), Lyman and Chatfield (1950),

and Hock (1958a) for curves of body temperature, oxygen consumption, and heart rate during arousal. At the end of 1½ to 3 hours the animal is fully active, with a normal high body temperature.

The reasons for periodic arousal are as yet unknown. Lowered levels of a nutrient substance as a possible cause for this phenomenon have been proposed (Hock, 1958b) (see Fig. 10). Kayser (1962), on the other hand, speculates that it is due to accumulation of a toxic substance. Pengelley and Fisher (1961) found that urine in the bladder was not responsible for the onset of arousal, as has often been theorized.

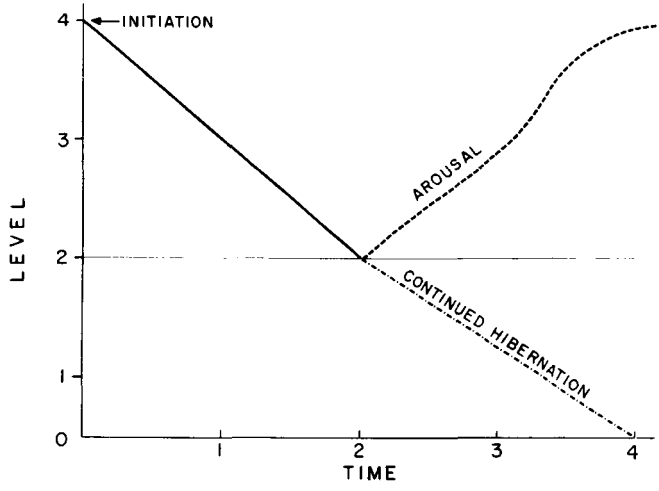

FIG. 10. Concept of cause of periodic arousal in hibernators. Nutrient substance is used during hibernation. At level 2, if animal continues hibernating all of nutrient is used, thus making arousal impossible. Therefore, nutrient is used to fuel arousal process, and more is converted from fat. Reprinted, with permission, from Hock (1958a).

N. Miscellaneous

There have been many studies made on mammals in hibernation, or mammals that hibernate, that do not fit under any of the preceding section headings. Some of these are indicated here, so that the interested student may refer to the techniques and findings.

The resistance of hibernating mammals to infection has been the subject of many older studies, and of a recent one by Kalabukhov (1958). Antigen disappearance in hibernating ground squirrels was studied by Jaroslow and Smith (1961). Chute (1960) found that helminths overwintered in the marmot, but Chute (1961) and Chute and Covalt (1960) found that *Trichinella spiralis* infections in golden hamsters and bats were

inhibited or retarded by hibernation. Sadler and Enright (1959) found that prolonged hibernation delayed rabies virus development in bats.

Lyman and Fawcett (1954) found sarcoma to be viable in hibernating hamsters for as long as 52 days, although proliferation did not occur until the animal became homoiothermic in a warm environment. Patterson *et al.* (1957) found the same picture in several tumors transplanted from man.

Kayser and Frank (1963), using radiographic and histological methods, studied the calcified tissues of the European hamster. During hibernation they found osteoporosis in the long and flat bones and particularly in the alveolar part of the jaw. Mayer and Bernick (1963) examined the effect of hibernation on the teeth and associated tissues in the Arctic ground squirrel and found increased dental caries, deficient dentinogenesis, and osteoporosis of the associated bones during hibernation. They postulated that these changes may be due to a demand for minerals, especially calcium, and that a consequent drain upon the teeth and bones is imposed during hibernation. Richardson *et al.* (1961), however, found no evidence that hibernation had either an adverse or a protective effect on the dental tissues. Periodontal tissue changes were found more frequently in laboratory-raised ground squirrels, hibernating or nonhibernating, than in wild animals.

X-irradiation has been studied by D. E. Smith (1958) and Brace (1952). F. Smith and Grenan (1951) found that, in hibernating marmots exposed to lethal doses of radiation, death did not occur until after arousal. Musacchia *et al.* (1963) studied effects of X-irradiation on tissue catecholamines of 13-lined ground squirrels.

Resistance of hibernators to hypoxia was discussed by Hiestand *et al.* (1950, 1953). Biörck *et al.* (1956a) studied reactions of hedgehogs to pure nitrogen, and mixtures of CO_2 and oxygen. Bullard *et al.* (1960) have discussed tolerance to hypoxia in hibernators. Although the relationship between hypoxia and hibernation is not definitively established, it is certain that animals in hibernation have a marked tolerance to hypoxia, or even to complete anoxia for at least 2 hours. The effect of high oxygen pressure was studied by V. Popovic *et al.* (1964), using 13-lined ground squirrels. Exposure to 6 atmospheres pure oxygen resulted in death of the hibernating animals in 18 hours. Artificially hypothermic animals survived only 6 hours, and normothermic animals only ½ hour. The oxygen consumptions for these three groups were in the ratio of 1 : 12 : 40, indicating that a lowered body temperature, with a concomitant decrease in metabolism, exerted a protective effect against high oxygen pressure.

Resistance to frostbite of hibernating ground squirrels is discussed by

Svihla (1955). P. and V. Popovic (1963) studied survival of newborn 13-lined ground squirrels after supercooling or freezing. After exposure to −6 to −8°C for 5 hours, 10 of the 12 2-day-old subject animals survived.

Zimny and Head (1961) studied effects of ultrasound on cardiac and skeletal muscle. Willis (1962) examined the resistance of tissues to cold swelling and found that this resistance is greater in the tissues of hibernating hamsters and ground squirrels than in those of the rat. Further, this resistance decreases in the hamster as the animal arouses.

Only a few studies have been made on behavior in hibernators. Panuska (1963) found no interest in heat reinforcement evoked by cooling chipmunks and 13-lined ground squirrels to 20°C. Kent and Popovic (1963) found a new circadian rhythm of activity induced by arousal from hibernation resulting in onset of activity at later than the normal time.

Ecological studies on mammals that hibernate rarely have much to do with this aspect of their life history. Kalabukhov (1960) has reviewed Russian work in this field. A notable paper by Bartholomew and Hudson (1961) should be referred to. Mayer (1953), Fitch (1948), Shaw (1925a), and Hamilton (1934) are other ecological references on, respectively: Arctic ground squirrel, Beechey ground squirrel, Columbian ground squirrel, and woodchuck.

The literature on hibernation is voluminous and often confusing, due to different conclusions on the same phenomenon. This is due, in part, to the fact that different species may be involved, with different pathways of response occurring. In part it may be due to slighter or greater variations in exposure to temperature, or varying techniques. For this reason, more recent studies are stressed here, although many of the older workers obtained admirable results. Furthermore, it has not always been realized that the depth and duration of hibernation may be factors in the response elicited by specific stimuli.

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